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=> d his

     (FILE 'HOME' ENTERED AT 12:50:58 ON 25 JUL 1999)
                SET COST OFF
                SET AUHELP OFF

     FILE 'HCAPLUS' ENTERED AT 12:51:06 ON 25 JUL 1999
                E SAPSE A/AU
L1            51 S E4-E6
                E STEROIDOGENESIS/PA,CS
L2             2 S E3-E7
L3            51 S L1,L2
L4          2273 S AZT OR ZIDUVUDINE
L5          1578 S DDC OR ZALCITABINE
L6           108 S NELFINAVIR
L7             1 S DELVIRDIN#
L8             0 S ABACARVIR#
                E ABACA
L9            24 S E13
                E DELVIR
L10           24 S EFAVIRENZ
L11           49 S ADEFOVIR?
L12            0 S BBH()10652
L13            0 S BBH()10 652
L14            0 S BBH10652
L15          253 S FTC
L16          283 S TBD
L17            0 S L15 AND L16
L18            1 S L16 AND 63/SC,SX
L19            0 S NKC482 OR NKC 482
L20            0 S NCK482 OR NCK 482
L21           83 S PMPA
L22            0 S POCPMPA
L23           11 S POC PMPA

     FILE 'BIOSIS' ENTERED AT 13:02:24 ON 25 JUL 1999
L24            0 S BBH10652 OR BBH()(10652 OR 10 652)

     FILE 'EMBASE' ENTERED AT 13:02:39 ON 25 JUL 1999
L25            0 S BBH10652 OR BBH()(10652 OR 10 652)

     FILE 'AIDSLINE' ENTERED AT 13:02:48 ON 25 JUL 1999
L26            0 S BBH10652 OR BBH()(10652 OR 10 652)
L27            2 S 10652

     FILE 'HCAPLUS' ENTERED AT 13:03:23 ON 25 JUL 1999
L28            0 S BCH10652 OR BCH()(10652 OR 10 652)

     FILE 'AIDSLINE' ENTERED AT 13:04:07 ON 25 JUL 1999
L29            0 S NCK482 OR NKC482 OR (NCK OR NKC)()482
L30            4 S TBD

     FILE 'REGISTRY' ENTERED AT 13:06:08 ON 25 JUL 1999
L31           13 S 30516-87-1 OR 7481-89-2 OR 69655-05-6 OR 3056-17-5 OR 134678-
                E BCH/CN
L32            1 S 143491-54-7
L33            2 S 143491-54-7/CRN
L34            1 S 66264-45-7
                E C38H66N2O2/MF
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L35          10 S E3
L36           4 S L35 AND 46.150.18/RID AND 2/NR
L37           2 S L36 NOT CYCLOHEXYL
L38           1 S L37 NOT 107004-47-7
L39           1 S L33 AND CLH
                E NKC/CN
                E NCK/CN
                E PMPA/CN
L40           1 S 147127-20-6
                E C 9H14N5O4P/MF
                E C9H14N5O4P/MF
L41          14 S E3 AND NCNC2-NCNC3/ES
L42           4 S L41 AND METHYLETHOXY METHYL
L43           3 S L42 AND 6 AMINO
L44           1 S 201341-05-1
                E C10N30N5O10P/MF
                E C19N30N5O10P/MF
                E C19H30N5O10P/MF
L45           1 S E3
L46          21 S L31,L32,L34,L38,L39,L40,L43,L45

     FILE 'HCAPLUS' ENTERED AT 13:16:00 ON 25 JUL 1999
L47        4563 S L46
L48        4334 S L4-L7,L9-L11,L15,L16,L21,L23
L49        4703 S PROCAINE
L50       40708 S ASCORBIC ACID
L51           4 S ZINC HEPTAHYDRATE
L52           2 S ZN HEPTAHYDRATE
L53       13958 S PHOSPHATIDYLSERINE
L54         246 S PHOSPHATIDYLSERINE(L)THU/RL
L55           4 S L54 AND HIV
L56         416 S HMB
L57           3 S L56 AND HIV
L58           3 S L56 AND IMMUNODEFICIEN?
L59           0 S L56 AND AIDS
L60        1722 S DHEA
L61        2175 S KETOCONAZOLE
L62        5074 S PREGNENOLONE
L63        4714 S PHENYTOIN
L64        8640 S CLONIDINE
L65         184 S IPRIFLAVONE
L66        1160 S RU 486

     FILE 'AIDSLINE' ENTERED AT 13:25:30 ON 25 JUL 1999
L67          10 S HMB

     FILE 'REGISTRY' ENTERED AT 13:25:55 ON 25 JUL 1999
L68           1 S 625-08-1

     FILE 'REGISTRY' ENTERED AT 13:26:34 ON 25 JUL 1999
L69           1 S 7440-66-6
L70         550 S 7440-66-6/CRN AND H2O
L71         524 S L70 AND 2/NC
L72           7 S L71 AND HEPTAHYDRATE
                E ZINC HEPTAHYDRATE/CN
                E ZN.7/MF
                E 7 H2O/MF
L73         543 S L70 NOT L72
L74         190 S L73 NOT (P OR N OR S OR SI OR MN OR CL OR B OR I OR F)/ELS
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L75         130 S L74 NOT C/ELS
L76           0 S L75 AND 3/ELC.SUB
L77          34 S L75 AND 3/ELC
L78          17 S L70 AND HEPTA?
L79          10 S L78 NOT L72,L77
L80          12 S 51-05-8 OR 50-81-7 OR L69 OR 73-78-9 OR 625-08-1 OR 53-43-0 O
L81           2 S L80 AND CLH
L82           2 S 137-58-6 OR 59-46-1
                E PHOSPHATIDYLSERINE/CN
                E ?PHOSPHATIDYLSERIN? NOT UNSPECIFIED
L83          38 S ?PHOSPHATIDYLSERIN?/CNS NOT UNSPECIFIED
L84          22 S L83 NOT SQL/FA
L85          36 S L80,L82,L84

     FILE 'HCAPLUS' ENTERED AT 13:38:36 ON 25 JUL 1999
L86      246490 S L85
L87      516565 S PROCAINE OR ASCORBIC ACID OR VITAMIN C OR ZINC OR ZN OR LIDOC
L88       27296 S DHEA OR DEHYDROEPIANDROSTERONE OR PRASTERONE OR KETOCONAZOLE
L89         213 S L86-L88 AND L48
L90          34 S L89 AND HIV
L91          18 S L89 AND AIDS
L92          36 S L89 AND (ACQUIR? OR HUMAN)()IMMUNODEFICIEN?

     FILE 'REGISTRY' ENTERED AT 13:42:20 ON 25 JUL 1999
L93           2 S 9068-38-6 OR 144114-21-6

     FILE 'REGISTRY' ENTERED AT 13:42:28 ON 25 JUL 1999

     FILE 'HCAPLUS' ENTERED AT 13:42:42 ON 25 JUL 1999
L94        6386 S L93
L95       14657 S REVERSE TRANSCRIPTASE OR REVTASE OR RETROPEPSIN
L96          11 S L89 AND L94,L95
L97          47 S L90-L92,L96
L98         588 S (ZN OR ZINC)(10A)(HEPTAHYDRATE OR 7H2O)
L99           7 S (ZN OR ZINC)()(HEPTAHYDRATE OR 7H2O)
                SEL RN

     FILE 'REGISTRY' ENTERED AT 13:45:04 ON 25 JUL 1999
L100         20 S E1-E20
L101          4 S L100 AND ZN/ELS
                E H7O7ZN/MF

     FILE 'HCAPLUS' ENTERED AT 13:46:38 ON 25 JUL 1999
L102          7 S L97 AND COMPOSITION
L103          9 S L89 AND (ACQUIR? OR HUMAN)(L)IMMUN#(L)DEFICIEN?
L104         47 S L97,L103
L105          7 S L104 AND COMPOSITION
L106          5 S L105 NOT ZINC FINGER
L107         16 S L104 AND COMBIN?
L108         14 S L107 NOT ZINC FINGER
L109          5 S L104 AND SYNERG?
L110          3 S L109 NOT ZINC FINGER
L111          2 S L104 AND FORMUL?
L112          2 S L111 NOT ZINC FINGER
L113         18 S L106,L108,L110,L112
L114          2 S L105,L107,L109 NOT L113
L115          3 S L89 AND MARROW
L116          1 S L89 AND ?NAUSE?
L117          0 S L89 AND (EMETIC OR ANTIEMETIC)
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L118          1 S L89 AND ?MYALG?
L119          0 S L89 AND (SLEEP OR INSOMN?)
L120          0 S L89 AND CUSHING#
L121          3 S L89 AND ?ANEMI?
L122          0 S L89 AND TRIGLYCER?
L123          3 S L89 AND ?CHOLESTEROL?
L124          3 S L89 AND INSULIN
L125          0 S L89 AND BUFFALO
L126         14 S L89 AND PROTEASE
L127          5 S L126 AND L94,L95
L128         12 S L126 AND L104
L129         18 S L115,L116,L118,L121,L123,L124,L127
L130         30 S L113,L129
L131          5 S L126,L128 NOT L130
L132          3 S L131 NOT (METALLOPROTEASE OR AMPRENAVIR)/TI
L133          3 S L132 AND L48
L134         33 S L130,L133
L135          0 S L3 AND L48
L136          5 S L3 AND L86-L88

     FILE 'REGISTRY' ENTERED AT 13:59:10 ON 25 JUL 1999
L137          1 S 51-05-8
L138          1 S 59-46-1
L139          1 S 50-81-7
L140          9 S 50-81-7/CRN AND 59-46-1/CRN
L141          1 S L140 AND ZN/ELS

     FILE 'HCAPLUS' ENTERED AT 13:59:55 ON 25 JUL 1999
L142          1 S L141
L143          5 S L136,L142
L144          5 S L143 NOT L134

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:00:21 ON 25 JUL 1999
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FILE COVERS 1967 - 25 Jul 1999  VOL 131 ISS 5
FILE LAST UPDATED: 24 Jul 1999  (19990724/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

 This file supports REG1stRY for direct browsing and searching of
 all substance data from the REGISTRY file.  Enter HELP FIRST for
 more information.


=> d all tot l144

L144 ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 1999 ACS
AN   1997:140247  HCAPLUS
```

DN 126:139888
TI Treatment of anemia, including HIV infection-associated anemia, with **procaine** compositions
IN **Sapse, Alfred T.**
PA **Steroidogenesis Inhibitors, Inc., USA**
SO PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9640038	A2	19961219	WO 1996-US5406	19960418

W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI US 1995-487038 19950607
AB The use of a **procaine** compn. to treat anemia, with particular applicability to the treatment of anemia assocd. with HIV infection, is disclosed. A **procaine/zinc/ascorbic acid**/potassium compn. for the treatment of anemia is also disclosed.
ST **zinc** ascorbate potassium **procaine** anemia treatment; HIV infection assocd anemia treatment **procaine**
IT T cell (lymphocyte)
(CD4+; **procaine** compns. for treatment of anemia, including HIV infection-assocd. anemia, in relation to increase of CD4 cell count)
IT AIDS (disease)
Anemia (disease)
Drug delivery systems
Human immunodeficiency virus
(**procaine** compns. for treatment of anemia, including HIV infection-assocd. anemia)
IT **50-81-7, Ascorbic acid**, biological studies
59-46-1, Procaine 7440-09-7, Potassium, biological studies **7440-66-6, Zinc**, biological studies
186646-39-9, Anticort
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**procaine** compns. for treatment of anemia, including HIV infection-assocd. anemia)

L144 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 1999 ACS
AN 1990:637859 HCAPLUS
DN 113:237859
TI Pharmaceutical composition containing a complexing agent and **procaine** for the treatment of symptoms from narcotic addiction, tinnitus, and Alzheimer's disease
IN **Sapse, Alfred T.**
PA USA
SO U.S., 4 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K027-00
NCL 514810000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4956391	A	19900911	US 1988-233247	19880817
	US 5064858	A	19911112	US 1990-578030	19900905
PRAI	US 1988-233247	19880817			

AB A compn. effective in reducing the withdrawal symptoms of recovering narcotic addicts and also in treating the symptoms of age-related conditions, such as tinnitus and Alzheimer's disease comprises **procaine** and a complexing agent, such as **ascorbic acid**, pantothenic acid, acetylsalicylic acid,and amino acids. The complexing agent prevents an unwanted hydrolysis of the **procaine** which would normally occur if the **procaine** is not protected. An injection soln. contained **procaine**-HCl 4, **ascorbic acid** 2 g, NaCl 14.652, chlorobutanol 16.65 mg, HCl/NaOH q.s., and water up to 100 mL.

ST narcotic addiction **procaine** complex injection; tinnitus Alzheimer disease **procaine** complex; ascorbate **procaine** tinnitus Alzheimer narcotic addiction

IT Narcotics
(addiction to, treatment of, with compn. contg. **procaine** and complexing agent)

IT Amino acids, biological studies
RL: BIOL (Biological study)
(narcotic addiction and age-related conditions treatment with compn. contg. **procaine** and)

IT Mental disorder
(Alzheimer's disease, treatment of, with compn. contg. **procaine** and complexing agent)

IT Hearing
(disorder, tinnitus, treatment of, with compn. contg. **procaine** and complexing agent)

IT Pharmaceutical dosage forms
(injections, of **procaine**, complexing agent in, for hydrolysis prevention)

IT **59-46-1, Procaine**
RL: BIOL (Biological study)
(narcotic addiction and age-related conditions treatment with compn. contg. complexing agent and)

IT 50-78-2 **50-81-7, Ascorbic acid**, biological studies 79-83-4, Pantothenic acid
RL: BIOL (Biological study)
(narcotic addiction and age-related conditions treatment with compn. contg. **procaine** and)

IT **57-41-0, Phenytoin 137-58-6, Lidocaine** 546-46-3, **Zinc** citrate **4205-90-7**
RL: BIOL (Biological study)
(narcotic addiction and age-related conditions treatment with compn. **procaine** and complexing agent and)

L144 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 1999 ACS
AN 1990:402025 HCAPLUS
DN 113:2025
TI Bacteriostatic and bactericidal composition and methods of use thereof
IN **Sapse, Alfred T.**
PA USA
SO PCT Int. Appl., 47 pp.

CODEN: PIXXD2
DT Patent
LA English
IC ICM A23B004-20
ICS A23B004-22; A23B004-24; A23B005-14; A23B005-16; A23B005-18; A23C003-08; C12N009-36
CC 5-2 (Agrochemical Bioregulators)
Section cross-reference(s): 17, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9004331	A1	19900503	WO 1989-US4576	19891013
	W: JP, US				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	EP 366869	A2	19900509	EP 1989-112992	19890714
	EP 366869	A3	19910612		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2000849	AA	19900417	CA 1989-2000849	19891017
PRAI	US 1988-258606		19881017		

AB The title compn. contains lysozyme and can be used for extension the shelf-life of fresh foods and milk and enhancing the antibacterial activity of denture cleaners and mouthwashes. The a lysozyme (5 mg) compn. prepd. from egg white, adjusted to pH 3.5 and contg. 15 ng **ascorbic acid** and 1.5 mg **Zn** showed strong antibacterial effect against Salmonella typhimurium, as compared to lysozyme compn. adjusted at pH 6.6. The antibacterial activity of lysozyme in fresh food, e.g. hamburger, mayonnaise, fish, juices, cabbage, chicken is reported. Denture cleaners and mouthwashes contg. lysozyme showed resistance against Candida albicans. The heat resistance of lysozyme was improved in the presence of the mineral component, e.g., **Zn** or I and the acid or acid-immunomodulating agent.

ST lysozyme bactericide food dental material
IT Beverages
Cheese
Egg yolk
Fish
Mayonnaise
Meat
Milk
(bactericides for, contg. lysozyme)
IT Oils, glyceridic
RL: BIOL (Biological study)
(bactericides for, contg. lysozyme)
IT Mineral elements
Amino acids, biological studies
Fatty acids, biological studies
Trace elements, biological studies
RL: BIOL (Biological study)
(lysozyme bacteriostatic and bactericidal compn. contg., for food and dental materials)
IT Dairy products
Egg white
(lysozyme from, bactericidal compns. contg.)
IT Bactericides, Disinfectants, and Antiseptics
Mouthwashes
(lysozyme-contg.)
IT Dentifrices
(denture cleansers, lysozyme-contg.)
IT Milk preparations

(yogurt, bactericides for, contg. lysozyme)
IT 9001-63-2, Lysozyme
RL: BIOL (Biological study)
(bacteriostatic and bactericidal compns. contg., for food and dental materials)
IT 50-78-2, Acetylsalicylic acid **50-81-7, Ascorbic acid**, biological studies 59-30-3, Folic acid, biological studies 60-33-3, Linoleic acid, biological studies 65-85-0, Benzoic acid, biological studies 79-83-4, Pantothenic acid 87-69-4, biological studies 124-07-2, Octanoic acid, biological studies 150-13-0, p-Aminobenzoic acid 7439-89-6, Iron, biological studies 7439-95-4, Magnesium, biological studies 7439-96-5, Manganese, biological studies 7440-24-6, Strontium, biological studies 7440-33-7, Tungsten, biological studies 7440-41-7, Beryllium, biological studies 7440-47-3, Chromium, biological studies 7440-50-8, Copper, biological studies 7440-56-4, Germanium, biological studies **7440-66-6, Zinc**, biological studies 7553-56-2, Iodine, biological studies 7782-49-2, Selenium, biological studies 9054-89-1
RL: BIOL (Biological study)
(lysozyme bacteriostatic and bactericidal compn. contg., for food and dental materials)
IT 1984-06-1, Sodium caprylate
RL: BIOL (Biological study)
(lysozyme bacteriostatic and bactericidal compns. contg., for food)

L144 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 1999 ACS
AN 1977:557198 HCAPLUS
DN 87:157198
TI Treating depression
IN **Sapse, Alfred T.**
PA Rom-Amer Pharmaceuticals, Ltd., USA
SO U.S., 9 pp.
CODEN: USXXAM
DT Patent
LA English
IC A61K031-245
NCL 424310000
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4041174	A	19770809	US 1974-498176	19740816

AB Injection and oral compns. for treating human depression contained a local anesthetic, an org. acid, a sulfite salt, and an acid salt. E.g., elderly patients with at least mild depressive disorders treated for 4 weeks with injections contg. **procaine**-HCl [**51-05-8**] 0.1000, benzoic acid [65-85-0] 0.0060, K2S2O5 0.0050, Na2HPO4 0.0005 g and water to make 5cc showed significant improvement.
ST anesthetic compn antidepressant
IT Antidepressants
(anesthetic-contg. compns.)
IT Anesthetics
(local, antidepressant compns. contg.)
IT 7558-79-4 16731-55-8
RL: BIOL (Biological study)
(in antidepressant compns.)
IT **51-05-8** 65-85-0, biological studies
RL: BIOL (Biological study)
(in pharmaceutical compn., for depressant treatment)

L144 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 1999 ACS
AN 1972:49949 HCAPLUS
DN 76:49949
TI Antibacterial lysozyme preparations
IN Crowell, Wilfred J.; **Sapse, Alfred T.**; Sercarz, Eli E.
PA Lysozyme Products, Inc.
SO Ger. Offen., 22 pp.
CODEN: GWXXBX
DT Patent
LA German
IC A61K
CC 63 (Pharmaceuticals)
Section cross-reference(s): 3
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2126204	A	19711209	DE 1971-2126204	19710526
	ES 391536	A1	19730616	ES 1971-391536	19710525
	FR 2100687	A5	19720324	FR 1971-18999	19710526
PRAI	US 1970-41119		19700527		

AB The title prepns., for oral and external use, e.g. as tooth pastes, mouth washes, eye drops, nasal sprays, skin moistening agents, food additives, and disinfectants, contained lysozyme (I), H2O2, and **ascorbic acid**, citric acid (II), tartaric acid, glycine, or cysteine. Thus, an aq. soln. contg. 100 .mu.g I/ml, 20 .mu.g II/ml, and 1 mg H2O2/ml caused 100% destruction of Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, and Bacillus subtilis after 30 min. A vaginal spray contained I.HCl 0.200, II 2.000, Na perborate 2.000, lactose 2.000, and balance H2O to 100.000 ml.
ST pharmaceutical lysozyme; antibacterial lysozyme compn; bladder rinsing lysozyme; tear artificial lysozyme; shampoo lysozyme; nasal spray lysozyme; acne lotion lysozyme; vaginal spray lysozyme
IT Bactericides, Disinfectants and Antiseptics
(lysozyme compns.)
IT 9066-59-5
RL: BIOL (Biological study)
(pharmaceutical bactericidal compns.)
IT **50-81-7**, biological studies 52-90-4, biological studies 77-92-9, biological studies 87-69-4 134-03-2 6000-43-7 7722-84-1, biological studies
RL: BIOL (Biological study)
(pharmaceutical bactericidal compns., contg. lysozyme)

=> sel hit rn l144
E1 THROUGH E8 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 14:00:34 ON 25 JUL 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 24 JUL 99 HIGHEST RN 228878-07-7
DICTIONARY FILE UPDATES: 24 JUL 99 HIGHEST RN 228878-07-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

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=> s e1-e8
             1 50-81-7/BI
               (50-81-7/RN)
             1 59-46-1/BI
               (59-46-1/RN)
             1 7440-66-6/BI
               (7440-66-6/RN)
             1 137-58-6/BI
               (137-58-6/RN)
             1 186646-39-9/BI
               (186646-39-9/RN)
             1 4205-90-7/BI
               (4205-90-7/RN)
             1 51-05-8/BI
               (51-05-8/RN)
             1 57-41-0/BI
               (57-41-0/RN)
L145         8 (50-81-7/BI OR 59-46-1/BI OR 7440-66-6/BI OR 137-58-6/BI OR
               186646-39-9/BI OR 4205-90-7/BI OR 51-05-8/BI OR 57-41-0/BI)

=> d ide can tot

L145 ANSWER 1 OF 8  REGISTRY  COPYRIGHT 1999 ACS
RN   186646-39-9  REGISTRY
CN   L-Ascorbic acid, mixt. with 2-(diethylamino)ethyl 4-aminobenzoate
     monohydrochloride, disodium hydrogen phosphate, potassium benzoate and
     zinc sulfate (1:1) (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Benzoic acid, 4-amino-, 2-(diethylamino)ethyl ester, monohydrochloride,
     mixt. contg. (9CI)
CN   Benzoic acid, potassium salt, mixt. contg. (9CI)
CN   Phosphoric acid, disodium salt, mixt. contg. (9CI)
CN   Sulfuric acid, zinc salt (1:1), mixt. contg. (9CI)
OTHER NAMES:
CN   Anticort
FS   STEREOSEARCH
MF   C13 H20 N2 O2 . C7 H6 O2 . C6 H8 O6 . Cl H . H3 O4 P . H2 O4 S . K . 2 Na
     . Zn
CI   MXS
SR   CA
LC   STN Files:   ADISINSIGHT, CA, CAPLUS, PHAR, TOXLIT

     CM   1

     CRN  7733-02-0  (7664-93-9)
     CMF  H2 O4 S . Zn
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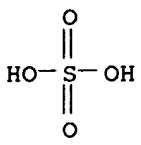
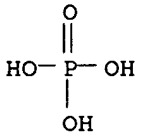


Zn

CM 2

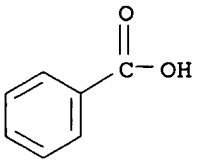
CRN 7558-79-4 (7664-38-2)
CMF H3 O4 P . 2 Na



2 Na

CM 3

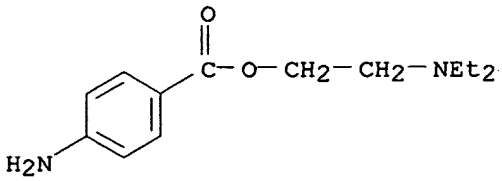
CRN 582-25-2 (65-85-0)
CMF C7 H6 O2 . K



● K

CM 4

CRN 51-05-8 (59-46-1)
CMF C13 H20 N2 O2 . Cl H

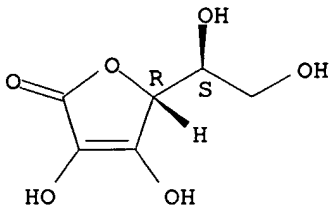


● HCl

CM 5

CRN 50-81-7
CMF C6 H8 O6

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:139888

L145 ANSWER 2 OF 8 REGISTRY COPYRIGHT 1999 ACS
RN **7440-66-6** REGISTRY
CN Zinc (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Asarco L 15
CN Blue powder
CN Ecka 4
CN F 1000
CN F 1000 (metal)
CN F 1500T
CN F 2000
CN F 2000 (metal)
CN LS 2
CN LS 2 (element)
CN LS 4
CN LS 5
CN LS 5 (metal)
CN NC-Zinc
CN Rheinzink
CN UF
CN UF (metal)
CN VM 4P16

DR 12793-53-2, 195161-85-4, 199281-21-5
MF Zn
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, APILIT, APILIT2, APIPAT, APIPAT2, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CHEMSAFE, CIN, CSCHEM, CSNB, DETHERM*, DDFU, DIPPR*, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA, ULIDAT, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Zn

181783 REFERENCES IN FILE CA (1967 TO DATE)
9568 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
181895 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:67336

REFERENCE 2: 131:67331

REFERENCE 3: 131:67328

REFERENCE 4: 131:67280

REFERENCE 5: 131:67278

REFERENCE 6: 131:67268

REFERENCE 7: 131:67263

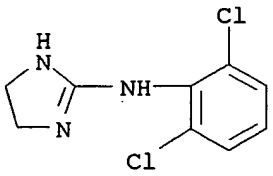
REFERENCE 8: 131:66996

REFERENCE 9: 131:66689

REFERENCE 10: 131:66476

L145 ANSWER 3 OF 8 REGISTRY COPYRIGHT 1999 ACS
RN **4205-90-7** REGISTRY
CN 1H-Imidazol-2-amine, N-(2,6-dichlorophenyl)-4,5-dihydro- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Imidazoline, 2-(2,6-dichloroanilino)- (7CI, 8CI)
OTHER NAMES:
CN 2-(2,6-Dichloroanilino)-2-imidazoline
CN 2-(2,6-Dichlorophenylimino)imidazolidine
CN 734571A
CN Clonidin
CN Clonidine
CN M 5041T
CN SKF 34427
FS 3D CONCORD
DR 57066-25-8, 138474-59-6

MF C9 H9 Cl2 N3
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CBNB, CIN, CSCHEM, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



5319 REFERENCES IN FILE CA (1967 TO DATE)
50 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5320 REFERENCES IN FILE CAPLUS (1967 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:63477

REFERENCE 2: 131:53959

REFERENCE 3: 131:53947

REFERENCE 4: 131:53868

REFERENCE 5: 131:53787

REFERENCE 6: 131:40048

REFERENCE 7: 131:39641

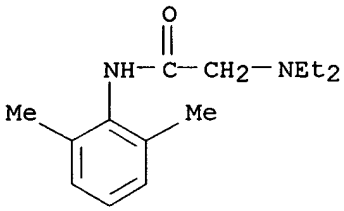
REFERENCE 8: 131:39633

REFERENCE 9: 131:39632

REFERENCE 10: 131:39585

L145 ANSWER 4 OF 8 REGISTRY COPYRIGHT 1999 ACS
RN **137-58-6** REGISTRY
CN Acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2',6'-Acetoxylidide, 2-(diethylamino)- (8CI)
OTHER NAMES:
CN .alpha.-Diethylamino-2,6-acetoxylidide
CN 2-(Diethylamino)-2',6'-acetoxylidide
CN Anbesol
CN Anestacon
CN Duncaine
CN Isicaina

CN Isicaine
CN Leostesin
CN Lidocaine
CN Lignocaine
CN Maricaine
CN Medicaine
CN Remicaine
CN Rucaina
CN Solcain
CN Xilina
CN Xycaine
CN Xylestesin
CN Xyline
CN Xylocain
CN Xylocaine
CN Xylocitin
FS 3D CONCORD
DR 8059-42-5, 8059-66-3, 91484-71-8
MF C14 H22 N2 O
CI COM
LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CBNB, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



5284 REFERENCES IN FILE CA (1967 TO DATE)
60 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5288 REFERENCES IN FILE CAPLUS (1967 TO DATE)
31 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:57355

REFERENCE 2: 131:53860

REFERENCE 3: 131:53599

REFERENCE 4: 131:49343

REFERENCE 5: 131:39648

REFERENCE 6: 131:39641

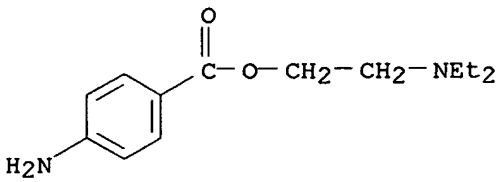
REFERENCE 7: 131:39571

REFERENCE 8: 131:39545

REFERENCE 9: 131:39442

REFERENCE 10: 131:39185

L145 ANSWER 5 OF 8 REGISTRY COPYRIGHT 1999 ACS
RN **59-46-1** REGISTRY
CN Benzoic acid, 4-amino-, 2-(diethylamino)ethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzoic acid, p-amino-, 2-(diethylamino)ethyl ester (8CI)
OTHER NAMES:
CN .beta.-(Diethylamino)ethyl p-aminobenzoate
CN .beta.-Diethylaminoethyl 4-aminobenzoate
CN 2-(Diethylamino)ethyl p-aminobenzoate
CN 2-Diethylaminoethyl 4-aminobenzoate
CN 4-Aminobenzoic acid 2-(diethylamino)ethyl ester
CN 4-Aminobenzoic acid diethylaminoethyl ester
CN Diethylaminoethyl p-aminobenzoate
CN Duracaine
CN Nissocaine
CN p-Aminobenzoic acid 2-diethylaminoethyl ester
CN Procain
CN Procaine
CN Procaine base
CN Spinocaine
CN Vitamin H3
FS 3D CONCORD
DR 91484-72-9
MF C13 H20 N2 O2
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DETHERM*, DDFU, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



2149 REFERENCES IN FILE CA (1967 TO DATE)
35 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2149 REFERENCES IN FILE CAPLUS (1967 TO DATE)
58 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:28213

REFERENCE 2: 131:27803

REFERENCE 3: 131:14954

REFERENCE 4: 131:13852

REFERENCE 5: 131:13848

REFERENCE 6: 131:13766

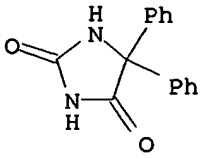
REFERENCE 7: 130:359083

REFERENCE 8: 130:335811

REFERENCE 9: 130:332708

REFERENCE 10: 130:332707

L145 ANSWER 6 OF 8 REGISTRY COPYRIGHT 1999 ACS
RN **57-41-0** REGISTRY
CN 2,4-Imidazolidinedione, 5,5-diphenyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Hydantoin, 5,5-diphenyl- (8CI)
OTHER NAMES:
CN 5,5-Diphenyl-2,4-imidazolidinedione
CN 5,5-Diphenylhydantoin
CN Aleviatin
CN Denyl
CN Di-Hydan
CN Di-Lan
CN Dihycon
CN Dilabid
CN Dintoina
CN Diphantoin
CN Diphedan
CN Diphenylan
CN Diphenylhydantoin
CN DPH
CN Hidantal
CN Lepitoin
CN Phenytoin
CN Phenytoine
CN Sodanton
CN Zentropil
FS 3D CONCORD
DR 125-59-7
MF C15 H12 N2 O2
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, ULIDAT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



5177 REFERENCES IN FILE CA (1967 TO DATE)
95 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5184 REFERENCES IN FILE CAPLUS (1967 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:63323

REFERENCE 2: 131:58758

REFERENCE 3: 131:56155

REFERENCE 4: 131:56144

REFERENCE 5: 131:54233

REFERENCE 6: 131:53892

REFERENCE 7: 131:53545

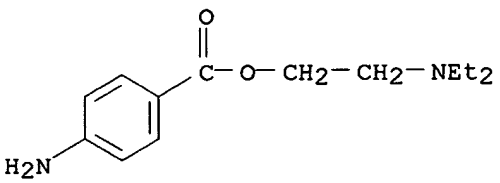
REFERENCE 8: 131:53535

REFERENCE 9: 131:53421

REFERENCE 10: 131:39647

L145 ANSWER 7 OF 8 REGISTRY COPYRIGHT 1999 ACS
RN **51-05-8** REGISTRY
CN Benzoic acid, 4-amino-, 2-(diethylamino)ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzoic acid, p-amino-, 2-(diethylamino)ethyl ester, monohydrochloride (8CI)
OTHER NAMES:
CN 2-Diethylaminoethyl p-aminobenzoate hydrochloride
CN Allocaine
CN Aminocaine
CN Anadolor
CN Anesthesol
CN Anestil
CN Atoxicocaine
CN Bernacaine
CN Cetain
CN Chlorocaine
CN Diethylaminoethanol 4-aminobenzoate hydrochloride
CN Ethocain
CN Ethocaine
CN Eugerase
CN Geriocaine
CN Gerovital H3
CN Herocaine

CN Irocaine
CN Isocain
CN Isocaine
CN Isocaine-Heisler
CN Juvocaine
CN Kerocaine
CN Lactocaine
CN Naucain
CN Naucaine
CN Neocaine
CN Neotonocaine
CN Novocain
CN Novocaine
CN Novocaine hydrochloride
CN Omnicain
CN Paracain
CN Planocaine
CN Polocaine
CN Procaine hydrochloride
CN Procaine monohydrochloride
CN Scurocaine
CN Sevicaine
CN Syncaine
CN Topokain
CN Westocaine
DR 12663-50-2, 8023-03-8, 138481-13-7, 41585-82-4
MF C13 H20 N2 O2 . Cl H
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CBNB, CIN, CSCHEM, DETHERM*, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (59-46-1)



● HCl

2243 REFERENCES IN FILE CA (1967 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2243 REFERENCES IN FILE CAPLUS (1967 TO DATE)
23 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:51393

REFERENCE 2: 131:39648

REFERENCE 3: 131:9619

REFERENCE 4: 130:301572

REFERENCE 5: 130:292512

REFERENCE 6: 130:245913

REFERENCE 7: 130:242300

REFERENCE 8: 130:242236

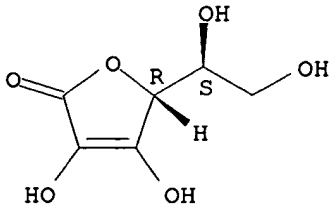
REFERENCE 9: 130:223871

REFERENCE 10: 130:223781

L145 ANSWER 8 OF 8 REGISTRY COPYRIGHT 1999 ACS
RN **50-81-7** REGISTRY
CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN (+)-Ascorbic acid
CN 3-keto-L-Gulofuranolactone
CN 3-Oxo-L-gulofuranolactone
CN Adenex
CN Allercorb
CN Antiscorbic vitamin
CN Antiscorbutic vitamin
CN Ascoltin
CN Ascorbajen
CN Ascorbic acid
CN Ascorbutina
CN Ascorin
CN Ascorteal
CN Ascorvit
CN C-Quin
CN C-Vimin
CN Cantan
CN Cantaxin
CN Catavin C
CN Ce-Mi-Lin
CN Ce-Vi-Sol
CN Cebicure
CN Cebion
CN Cebione
CN Cecon
CN Cegiolan
CN Ceglion
CN Celaskon
CN Celin
CN Cemagyl
CN Cenetone
CN Cereon
CN Cergona
CN Cescorbat
CN Cetamid
CN Cetemican
CN Cevalin

CN Cevatine
CN Cevex
CN Cevimin
CN Cevital
CN Cevitamic acid
CN Cevitamin
CN Cevitan
CN Cevitex
CN Chewcee
CN Ciamin
CN Cipca
CN Citrovit
CN Colascor
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS STEREOSEARCH
DR 56533-05-2, 57304-74-2, 57606-40-3, 56172-55-5, 129940-97-2, 14536-17-5, 50976-75-5, 89924-69-6, 30208-61-8
MF C6 H8 O6
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, APILIT, APILIT2, APIPAT, APIPAT2, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CIN, CSCHEM, CSNB, DETHERM*, DDFU, DIPPR*, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, TULSA, ULIDAT, USAN, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



37531 REFERENCES IN FILE CA (1967 TO DATE)
898 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
37563 REFERENCES IN FILE CAPLUS (1967 TO DATE)
12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:67338

REFERENCE 2: 131:67290

REFERENCE 3: 131:67223

REFERENCE 4: 131:64872

REFERENCE 5: 131:64860

REFERENCE 6: 131:63564

REFERENCE 7: 131:63539

REFERENCE 8: 131:63471

REFERENCE 9: 131:63463

REFERENCE 10: 131:63317

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:01:22 ON 25 JUL 1999
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1967 - 25 Jul 1999 VOL 131 ISS 5
FILE LAST UPDATED: 24 Jul 1999 (19990724/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> d bib abs hitrn tot l134

L134 ANSWER 1 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1999:103039 HCAPLUS
DN 130:332308
TI Clinical experience and choice of drug therapy for **human immunodeficiency** virus disease
AU Brosgart, Carol L.; Mitchell, Thomas F.; Coleman, Rebecca L.; Dyner, Toby; Stephenson, Kathryn E.; Abrams, Donald I.
CS Community Consortium, University of California San Francisco AIDS Program at San Francisco General Hospital, San Francisco, CA, USA
SO Clin. Infect. Dis. (1999), 28(1), 14-22
CODEN: CIDIEL; ISSN: 1058-4838
PB University of Chicago Press
DT Journal
LA English
AB To det. if providers experienced in the management of **human immunodeficiency** virus (**HIV**) disease preferred different treatment regimens than providers with less experience, we analyzed data from a national survey of primary care providers' preferred regimens for the management of 30 **HIV**-related medical conditions. We mailed questionnaires to 999 correct addresses of providers in > 20 cities in the United States in May 1996. We received 524 responses (response rate, 52%). We found a statistically significant assocn. between the no. of **HIV**-infected patients cared for by the provider and the likelihood that the provider would report prescribing highly active antiretroviral therapy and multidrug **combinations** for treatment of opportunistic infections. Providers with few **HIV**-infected patients were substantially less likely to report using new therapeutic regimens or new diagnostic tools. We concluded that the preferred regimens of experienced providers are more likely to be consistent with the latest information on treatment for **HIV** disease than are those of less experienced providers.
IT **9068-38-6, Reverse transcriptase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; mono- and **combination** antiretroviral therapy for

HIV-related disease and prophylaxis for opportunistic infections: clin. experience)

IT **65277-42-1, Ketoconazole**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mono- and **combination** antiretroviral therapy for **HIV**-related disease and prophylaxis for opportunistic infections: clin. experience)

L134 ANSWER 2 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:749754 HCAPLUS
DN 130:119007
TI Prediction of aryl hydrocarbon receptor-mediated enzyme induction of drugs and chemicals by mRNA quantification
AU Froetschl, Roland; Chichmanov, Lubomir; Kleeberg, Ullrich; Hildebrandt, Alfred G.; Roots, Ivar; Brockmoeller, Juergen
CS Institute of Clinical Pharmacology, University Hospital Charite, Berlin, D-10098, Germany
SO Chem. Res. Toxicol. (1998), 11(12), 1447-1452
CODEN: CRTOEC; ISSN: 0893-228X
PB American Chemical Society
DT Journal
LA English
AB Enzyme-specific testing for drug interactions by in vitro techniques has become a routine practice in drug development. With many drugs, enzyme induction has similar importance for the prediction of drug-drug interactions. The authors developed a method for recognizing enzyme induction mediated via the aryl hydrocarbon receptor. This type of induction may be clin. important since exptl. data suggest a higher rate of toxification in induced subjects. Twenty-four drugs and environmental chems., selected as prototype inducers or being chem. related to known inducers, including HIV **protease** inhibitors **nelfinavir**, saquinavir, ritonavir, and indinavir, were tested for their potency to induce cytochrome P 450 1A1 mRNA in human Hela cell cultures by a quant. **reverse transcriptase** polymerase chain reaction. Known prototype inducers such as .beta.-naphthoflavone and 3-methylcholanthrene exhibited the highest inducing potency quantified with an Imax value (maximal induction of cytochrome P 450 1A1 mRNA synthesis) of 5.48 and 10.7 .times. 106 mRNA mols. per 150 ng of total RNA, resp. The enzyme-inducing efficacy of some compds. such as resveratrol (2.92 .times. 106) and the **protease** inhibitors was not much lower (2.23-3.08 .times. 106). All compds. that were structurally similar to benzimidazoles exhibited some extent of enzyme induction; e.g., Imax values were 0.86 .times. 106, 0.20 .times. 106, and 0.14 .times. 106 for omeprazole, lansoprazole, and losartan, resp. To predict the clin. relevance of these inducing effects, the concn. at half-maximal induction IM was estd.; the plasma concns. of these drug substances were within 1 order of magnitude of the IM values, upon usual dosage. In conclusion, cytochrome P 450 1A1 enzyme induction by drugs is a common phenomenon, though there is a great range in the inducing efficacy. In vitro prediction of enzyme induction may be useful for explaining or foreseeing drug interactions, drug side effects, or toxicity by xenobiotics.

IT **57-41-0, Phenytoin**
RL: ANT (Analyte); ANST (Analytical study)
(prediction of aryl hydrocarbon receptor-mediated enzyme induction of drugs and chems. by mRNA quantification)

L134 ANSWER 3 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:741808 HCAPLUS

DN 130:133613
TI Ritonavir: clinical pharmacokinetics and interactions with other anti-**HIV** agents
AU Hsu, Ann; Granneman, G. Richard; Bertz, Richard J.
CS Abbott Laboratories, Abbott Park, IL, USA
SO Clin. Pharmacokinet. (1998), 35(4), 275-291
CODEN: CPKNDH; ISSN: 0312-5963
PB Adis International Ltd.
DT Journal
LA English
AB Ritonavir is 1 of the 4 potent synthetic **HIV** protease inhibitors, approved by the US Food and Drug Administration (FDA) between 1995 and 1997, that have revolutionized **HIV** therapy. The extent of oral absorption is high and is not affected by food. Within the clin. concn. range, ritonavir is approx. 98 to 99% bound to plasma proteins, including albumin and .alpha.1-acid glycoprotein. Cerebrospinal fluid (CSF) drug concns. are low in relation to total plasma concn. However, parallel decreases in the viral burden have been obsd. in the plasma, CSF and other tissues. Ritonavir is primarily metabolized by cytochrome P 450 (CYP) 3A isoenzymes and, to a lesser extent, by CYP2D6. Four major oxidative metabolites have been identified in humans, but are unlikely to contribute to the antiviral effect. About 34% and 3.5% of a 600mg dose is excreted as unchanged drug in the feces and urine, resp. The clin. relevant t1/2.beta. is about 3 to 5 h. Because of auto-induction, plasma concns. generally reach steady state 2 wk after the start of administration. The pharmacokinetics of ritonavir are relatively linear after multiple doses, with apparent oral clearance averaging 7 to 9 L/h. In vitro, ritonavir is a potent inhibitor of CYP3A. In vivo, ritonavir significantly increases the AUC of drugs primarily eliminated by CYP3A metab. (e.g. clarithromycin, **ketoconazole**, rifabutin, and other **HIV** protease inhibitors, including indinavir, saquinavir and **nelfinavir**) with effects ranging from an increase of 77% to 20-fold in humans. It also inhibits CYP2D6-mediated metab., but to a significantly lesser extent (145% increase in desipramine AUC). Since ritonavir is also an inducer of several metabolizing enzymes [CYP1A4, glucuronosyl transferase (GT), and possibly CYP2C9 and CYP2C19], the magnitude of drug interactions is difficult to predict, particularly for drugs that are metabolized by multiple enzymes or have low intrinsic clearance by CYP3A. For example, the AUC of CYP3A substrate methadone was slightly decreased and alprazolam was unaffected. Ritonavir is minimally affected by other CYP3A inhibitors, including **ketoconazole**. Rifampicin (rifampin), a potent CYP3A inducer, decreased the AUC of ritonavir by only 35%. The degree and duration of suppression of **HIV** replication is significantly correlated with the plasma concns. Thus, the large increase in the plasma concns. of other protease inhibitors when coadministered with ritonavir forms the basis of rational dual protease inhibitor regimens, providing patients with 2 potent drugs at significantly reduced doses and less frequent dosage intervals. **Combination** treatment of ritonavir with saquinavir and indinavir results in potent ans sustained clin. activity. Other important factors with **combination** regimens include reduced interpatient variability for high clearance agents, and elimination of the food effect on the bioavailability of indinavir.
IT **65277-42-1, Ketoconazole**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ritonavir pharmacokinetics and interactions with other anti-**HIV** agents in humans)

L134 ANSWER 4 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:488721 HCAPLUS
DN 129:211257
TI Characterization of the selectivity and mechanism of human cytochrome P450 inhibition by the **human immunodeficiency** virus-**protease** inhibitor **nelfinavir** mesylate
AU Lillibridge, James H.; Liang, Bai Hong; Kerr, Bradley M.; Webber, Stephanie; Quart, Barry; Shetty, Bhasker V.; Lee, Caroline A.
CS Agouron Pharmaceuticals Inc., USA
SO Drug Metab. Dispos. (1998), 26(7), 609-616
CODEN: DMDSAI; ISSN: 0090-9556
PB Williams & Wilkins
DT Journal
LA English
AB In vitro studies with human liver microsomes and P 450 probe substrates were performed to characterize selectivity and mechanism of cytochrome P 450 inhibition by **nelfinavir** mesylate. At therapeutic concns. (steady-state plasma concns. .apprx.4 .mu.M), **nelfinavir** was found to be a competitive inhibitor of only testosterone 6.beta.-hydroxylase (CYP3A4) with a K, concn. of 4.8 .mu.M. At supratherapeutic concns., **nelfinavir** competitively inhibited dextromethorphan O-demethylase (CYP2D6), S-mephenytoin 4-hydroxylase (CYP2C19), and phenacetin O-deethylase (CYP1A2) with K, concns. of 68, 126, and 190 .mu.M, resp. **Nelfinavir** did not appreciably inhibit tolbutamide 4-hydroxylase (CYP2C9), paclitaxel 6.alpha.-hydroxylase (CYP2C8), or chlorzoxaxone 6.beta.-hydroxylase (CYP2E1) activities. The inhibitory potency of **nelfinavir** toward CYP3A4 suggested the possibility of in vivo inhibition of this isoform, whereas in vivo inhibition of other P450s was considered unlikely. In a one-sequence crossover study in 12 healthy volunteers, **nelfinavir** inhibited the elimination of the CYP3A substrate terfenadine and the carboxylate metabolite of terfenadine. The 24-h urinary recoveries of 63-hydroxycortisol were reduced by an av. of 27% during **nelfinavir** treatment, consistent with CYP3A inhibition by **nelfinavir**. Inhibition of CYP3A4 by **nelfinavir** in vitro was NADPH-dependent requiring the catalytic formation of a metabolite or a metabolic intermediate. The catechol metabolite of **nelfinavir** (M3) was considered unlikely to be responsible for inhibition as the addn. of catechol O-Me transferase, S-adenosyl methionine, and **ascorbic acid** to the pre-incubation mixt. did not protect against the loss of testosterone 6.beta.-hydroxylase activity. Also, the addn. of M3 to human liver microsomes did not inhibit CYP3A4. Although incubations with **nelfinavir** showed a time- and concn.-dependent loss of CYP3A4 activity, the partial or complete recovery of enzyme activity upon dialysis indicated that inhibition was reversible. Microsomal incubations with **nelfinavir** and NADPH did not result in a loss of spectral P 450 content compared with the NADPH control. Glutathione, N-acetylcysteine, and catalase did not attenuate CYP3A4 inhibition by **nelfinavir**. Collectively, these results suggest that the probable mechanism for CYP3A4 inhibition by **nelfinavir** is a transient metabolic intermediate or stable metabolite that coordinates tightly but reversibly to the heme moiety of the P 450.

L134 ANSWER 5 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:462003 HCAPLUS
DN 129:239301
TI **Nelfinavir**: a review of its therapeutic efficacy in **HIV** infection

AU Jarvis, Blair; Faulds, Diana
CS Adis International Limited, Auckland, N. Z.
SO Drugs (1998), 56(1), 147-167
CODEN: DRUGAY; ISSN: 0012-6667
PB Adis International Ltd.
DT Journal; General Review
LA English
AB A review with 98 refs. **Nelfinavir** is a selective inhibitor of **HIV protease**, the enzyme responsible for post-translational processing of **HIV** propeptides. In the presence of the drug, immature, noninfectious virus particles are produced. **Nelfinavir** in **combination** with nucleoside **reverse transcriptase** inhibitors (NRTIs), non-nucleoside **reverse transcriptase** inhibitors and/or other **protease** inhibitors profoundly suppresses viral replication. Plasma **HIV** RNA levels (viral load) rapidly fall below the limit of detection (LOD; usually 400 or 500 copies/mL) in the majority of patients. When used in **combination** with NRTIs, **nelfinavir** 1250mg twice daily produced similar results to 3-times-daily **nelfinavir** at a range of total daily dosages. In an ongoing study >70% of adults receiving a **nelfinavir**-based **combination** regimen had plasma **HIV** RNA levels below the LOD (<400 copies/mL) after 84 wk. In addn., 73% of pediatric patients receiving **nelfinavir** plus at least 1 new NRTI had viral loads below the LOD (<400 copies/mL) after 34 wk. Furthermore, CD4+ cell counts generally increased in conjunction with redns. in viral load. **Combination** therapy with **nelfinavir** and saquinavir results in higher saquinavir plasma concns., makes twice-daily administration of saquinavir feasible and may delay the emergence of resistant viral strains. A unique mutation at codon 30 (D30N) of the **protease** gene confers resistance to **nelfinavir**, but **HIV** with the D30N mutation remains fully susceptible to indinavir, ritonavir and saquinavir in vitro. Nonetheless, in clin. use, significant cross-resistance is seen with all currently available **protease** inhibitors. Diarrhoea is the most frequently reported adverse event in patients receiving **nelfinavir**-based **combination** therapy and has been reported in up to 32% of **nelfinavir** recipients in randomized trials. Diarrhoea is generally of mild to moderate severity and does not result in wt. loss. Rash, **nausea** , headache and asthenia were each reported in .ltoreq.5% of patients. Approx. 5% of patients enrolled in an expanded access program in the US discontinued **nelfinavir** because of adverse events. **Nelfinavir** is metabolized by the cytochrome P 450 system. Several clin. significant pharmacokinetic drug interactions between **nelfinavir** and other drugs (i.e. **ketoconazole**, rifabutin, rifampicin), including other **protease** inhibitors (i.e. indinavir, ritonavir, saquinavir) have been documented. As with other available **protease** inhibitors, hyperglycemia, hyperlipidemia and abnormal fat distribution have been reported, albeit infrequently, in assocn. with **nelfinavir**. **Nelfinavir** -based **combination** regimens are well tolerated and produce profound and prolonged suppression of **HIV** replication in adult and paediatric patients. Hence, **nelfinavir** is suitable for inclusion in antiretroviral regimens for initial therapy for **HIV** infection and, alternatively, in regimens for patients unable to tolerate other **protease** inhibitors.

L134 ANSWER 6 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:436291 HCAPLUS

DN 129:183826
TI Zidovudine azido-reductase in human liver microsomes: activation by ethacrynic acid, dipyridamole, and indomethacin and inhibition by **human immunodeficiency** virus **protease** inhibitors
AU Fayz, Shirin; Inaba, T.
CS Department Pharmacolog, Faculty Medicine, University Toronto, Toronto, ON, M5S1A8, Can.
SO Antimicrob. Agents Chemother. (1998), 42(7), 1654-1658
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB **AZT** (zidovudine, 3'-azido-3'-deoxythymidine), although metabolized primarily to **AZT**-glucuronide, is also metabolized to 3'-amino-3'-deoxythmidine (AMT) by redn. of the azide to an amine. The formation of the myelotoxic metabolite AMT has not been well characterized, but inhibition of AMT formation would be of therapeutic benefit. The aim of this study was to identify compds. that inhibit AMT formation. Using human liver microsomes under anaerobic conditions and [2-14C]**AZT**, Km values of **AZT** azido-reductase, estd. by radio-thin-layer chromatog., were 2.2 to 3.5 mM. Oxygen completely inhibited this NADPH-dependent redn. Thirteen of the 28 compds. tested inhibited the formation of AMT. In addn. to the CYP3A4 inhibitors **ketoconazole**, fluconazole, indinavir, ritonavir, and saquinavir, metyrapone strongly inhibited AMT formation. An unexpected finding was the more-than-twofold increase in AMT formation in the presence of ethacrynic acid, dipyridamole, or indomethacin. Such activation of toxic metabolite formation would impair drug therapy.
IT **65277-42-1, Ketoconazole**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(zidovudine azido-reductase in human liver microsomes and activation by ethacrynic acid and dipyridamole and indomethacin and inhibition by **human immunodeficiency** virus **protease** inhibitors)

L134 ANSWER 7 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:213357 HCAPLUS
DN 128:289783
TI **Protease** inhibitors as inhibitors of human cytochromes P450: high risk associated with ritonavir
AU Von Moltke, Lisa L.; Greenblatt, David J.; Grassi, Jeffrey M.; Granda, Brian W.; Duan, Su Xiang; Fogelman, Steven M.; Daily, Johanna P.; Harmatz, Jerold S.; Shader, Richard I.
CS Department of Pharmacology and Experimental Therapeutics and the Division of Clinical Pharmacology, Tufts University School of Medicine and New England Medical Center, Boston, MA, 02111, USA
SO J. Clin. Pharmacol. (1998), 38(2), 106-111
CODEN: JCPCBR; ISSN: 0091-2700
PB Lippincott-Raven Publishers
DT Journal
LA English
AB Four **protease** inhibitor antiviral agents (ritonavir, indinavir, **nelfinavir**, saquinavir) were evaluated as in vitro inhibitors of the activity of six human cytochromes using an in vitro model based on human liver microsomes. Ritonavir was a highly potent inhibitor of P 450-3A activity (triazolam hydroxylation), having inhibitory potency slightly less than **ketoconazole**. Indinavir was also a potent 3A

inhibitor, while **nelfinavir** and saquinavir were less potent. Ritonavir had high inhibition potency against cytochrome P 450-2C9 (tolbutamide hydroxylation), -2C19 (S-mephenytoin hydroxylation), and -2D6 (dextromethorphan O-demethylation and desipramine hydroxylation), while the other **protease** inhibitors had one or more orders of magnitude lower inhibitory activity against these reactions. None of the **protease** inhibitors had important inhibitory potency against P 450-1A2 (phenacetin O-deethylation) or -2E1 (chlorzoxazone hydroxylation). Thus, among available **protease** inhibitors, ritonavir carries the highest risk of incurring drug interactions due to inhibition of cytochrome P 450 activity.

L134 ANSWER 8 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:180782 HCAPLUS
DN 128:256389
TI Immune direction therapy
IN Prendergast, Patrick T.
PA Prendergast, Patrick T., Ire.
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9810787	A2	19980319	WO 1997-IB1086	19970910
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9741320	A1	19980402	AU 1997-41320	19970910
	SE 9900812	A	19990308	SE 1999-812	19990308
PRAI	US 1996-25180	19960911			
	WO 1997-IB1086	19970910			

AB Herein is described a specific amino acid sequence which exhibits specific ion (bridge) pair arrays enclosed on at least one side by non polar hydrophobic transmembrane segments, as a mechanism used by many infectious agents and a no. of cytokine inhibitory factors, such as interleukin 10 and prolactin inhibitory factor and alpha-fetoprotein, to not only undermine the hosts **immune** defences but to also allow for the infection of target lymphoid tissue. It has been demonstrated that certain vaccines, when inoculated into a host, produced a range of neutralizing antibodies but failed to prevent infection when that host is later challenged with live infectious organism. This present patent illustrates that when such vaccine inoculation is coupled with passive immunization with mono or polyclonal antibodies to these specific amino acid sequences as specified herein that the host is then capable of overcoming the infectious challenge. Herein is described the therapeutic use of mono or polyclonal antibodies to these said specific sequences as a treatment for **acquired immune deficiency** syndrome (**AIDS**) and other disease states that persist due to the presence of a cytokine inhibitory factor of viral, fungal, bacterial or host origin such as chronic fatigue syndrome where interleukin 10 mimic mols. are responsible for a multitude of disease symptoms identified as indicative of **myalgic** encephalitis. Herein is described the

therapeutic use of mono or polyclonal antibodies to these specific amino acid sequences as a **combination** therapy with vaccines and anti-viral agents to prevent side effects from certain **immune** modulation and anti-viral agents (e.g. **DHEA** and IL-12) which cause enhanced prodn. of Interleukin 10 or AFP mimic mols. during therapy. Also herein is described the therapeutic use of these specific sequences either isolated from the organism source or produced by direct synthesis or recombinant protein synthesis. These peptides when administered to a patient suffering from an autoimmune disease, such as multiple sclerosis (MS), lupus (systemic lupus erythematosus) or diabetes or rheumatoid arthritis as limited examples or to transplant organ recipients, will allow the patient's **immune** state to be shifted to a Th2 antibody dependent **immune** response and curtail the Th1 (T cell dependent) **immune** attack which is evident in such **immune** malfunctions as MS and graft vs. host disease. Certain dermatol. conditions which are today treated by the use of corticosteroid creams and ointment may also be successfully treated by replacing the corticosteroid with these mimic immunosuppressive AFP/interleukin 10 sequences outlined in this patent.

L134 ANSWER 9 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1998:65902 HCAPLUS
DN 128:123799
TI Antiviral pharmaceutical compositions containing saturated 1,2-dithiaheterocyclic compounds, and uses thereof
IN Rice, William G.; Schultz, Robert R.; Baker, David C.; Henderson, Louis E.
PA United States Dept. of Health and Human Services, USA; University of Tennessee Research Corp.; Rice, William G.; Schultz, Robert R.; Baker, David C.; Henderson, Louis E.
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9801440	A2	19980115	WO 1997-US10870	19970703
	WO 9801440	A3	19980514		
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9744085	A1	19980202	AU 1997-44085	19970703
PRAI	US 1996-21665	19960705			
	WO 1997-US10870	19970703			

OS MARPAT 128:123799
AB Pharmaceutical compns. including a satd. 1,2-dithiaheterocyclic compd. having antiviral activity are provided. Also provided are a kit contg. the pharmaceutical compn. and methods of treating or preventing viral disease using the compn., as well as methods for inactivating a retrovirus in a body fluid.

L134 ANSWER 10 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:499199 HCAPLUS

DN 127:181141
TI Protein occlusion for delivery of small molecules
IN Panayotatos, Nikos
PA Panayotatos, Nikos, USA
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9726275	A1	19970724	WO 1997-US675	19970116
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9722428	A1	19970811	AU 1997-22428	19970116
	EP 886649	A1	19981230	EP 1997-905579	19970116
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1996-9804 19960116
WO 1997-US675 19970116
AB The present invention relates to complexes between (1) a target-binding moiety; (2) a cavity-forming moiety; and (3) a pharmacol. compd. to be delivered to a target, wherein the pharmacol. compd. is buried inside of the cavity-forming moiety, but not covalently bound to either the target-binding moiety or the cavity-forming moiety. The complexes of this invention may be used as to deliver a pharmacol. compd. to cells, tissues, organs, viruses, microorganisms or other surfaces that are characterized by an entity that binds the target-binding moiety portion of the complex. The present invention also relates to pharmaceutical **compns.** comprising the non-covalent complexes of this invention. The invention also relates to methods of delivering a pharmacol. compd. to a target in a patient. The present invention also relates to the use of the complexes of this invention for the sepn. of chem. entities from their chiral forms or contaminants.
IT **7440-66-6, Zinc,** biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(protein occlusion for delivery of small mols.)

L134 ANSWER 11 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:332397 HCAPLUS
DN 126:301796
TI Use of 2-mercaptoethanolamine (2-MEA) and related aminothiol compounds and copper(II)-3,5 diisopropyl salicylates and related compounds in the prevention and treatment of **AIDS**, cancer, autoimmune disease, microbiological infections, and other diseases
IN Chachoua, Samir
PA Chachoua, Samir, Mex.
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9711666	A2	19970403	WO 1996-IB1059	19960925
	WO 9711666	A3	19970619		
	W: AL, AM, AU, BB, BG, BR, CA, CN, CU, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2233015	AA	19970403	CA 1996-2233015	19960925
	CA 2233445	AA	19970403	CA 1996-2233445	19960925
	AU 9669990	A1	19970417	AU 1996-69990	19960925
	EP 858327	A2	19980819	EP 1996-931214	19960925
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1995-4281	19950925			
	WO 1996-IB1059	19960925			

AB New therapeutic **compns.** and applications of 2-MEA and related aminothiols and copper(II)-3,5-diisopropyl salicylates, solely or in **combination** with other factors, agents, or processes that are phys., chem. and/or biol.-based, are disclosed. These include precursors, intermediates, end products, catalysts, promoters and/or any factors, agents, or processes involved directly or indirectly from initial application of the **compns.** to the final result. The methods and **compns.** of the invention are useful for the treatment of **AIDS**, cancer, autoimmune disease, and microbiol. infections, as well as other diseases in which immunol. dysfunction and/or free radical formation function as part of the disease mechanism.

IT **50-81-7, Vitamin C**, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mercaptoethanolamine, related aminothiols, copper diisopropyl salicylate, and related compds., alone or in **combination**, for prevention and treatment of disease)

L134 ANSWER 12 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:329346 HCAPLUS
DN 126:303447
TI Biologically-active polymers
IN Katoot, Mohammad W.
PA Katoot, Mohammad W., USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9712989	A1	19970410	WO 1996-US15828	19961002
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	CA 2233059	AA	19970410	CA 1996-2233059	19961002

AU 9672535 A1 19970428 AU 1996-72535 19961002
EP 882139 A1 19981209 EP 1996-934013 19961002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1995-4757 19951002
US 1996-599888 19960212
US 1996-22825 19960726
US 1996-724461 19961001
WO 1996-US15828 19961002

AB This invention relates to biol.-active polymers that are useful for analyte detection and isolation and delivery of substances. The biol.-active polymers are capable of specifically and reversibly binding to analytes, including mols. and cells. The biol.-active polymers are also capable of releasing substances upon elec. stimulation. The present invention provides compns. comprising biol.-active polymers membranes and methods for making these biol.-active polymers membranes that may be specifically designed to selectively bind cells and specific cell types, to affect cell growth characteristics, and to modulate cellular differentiation. These biol.-active polymer membranes may be controlled elec. to induce controlled cellular differentiation and modulate the cell growth cycle. These biol.-active polymers have many applications in biol. and chem. fields.

IT **65277-42-1, Ketoconazole**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(biol. active polymers useful for analyte detection and isolation and delivery of substances)

L134 ANSWER 13 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:318204 HCAPLUS
DN 126:292446
TI Therapeutic applications of animal sera including horse serum in the treatment of **AIDS**, cancer, and other viral and bacterial diseases
IN Chachoua, Samir
PA Chachoua, Samir, Mex.
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9711667	A2	19970403	WO 1996-IB1115	19960925
WO 9711667	A3	19970612		

W: AL, AM, AU, BB, BG, BR, CA, CN, CU, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2233015	AA	19970403	CA 1996-2233015	19960925
CA 2233445	AA	19970403	CA 1996-2233445	19960925
AU 9671431	A1	19970417	AU 1996-71431	19960925
EP 853486	A2	19980722	EP 1996-932773	19960925

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1995-4281 19950925

WO 1996-IB1115 19960925

AB Animal (e.g. horse) antisera raised by using target organism or target organism-contg. patient cell is washed with patient's red blood cell, and used together with pharmaceuticals for treating disease. The target organism and cell includes **AIDS** virus, **HIV**, herpes, cytomegalovirus, pneumocystis, cancer cell, virus, bacteria, etc. The disease include **AIDS**, opportunistic infections, cancer, and viral or bacterial diseases. The pharmaceuticals **combination** is selected from **AZT**, DDI, 2-MEA, BHT, antibiotic, chemotherapeutic agent, radiotherapeutic agent, transfer factor, death sequence factor, antigen, fibroblast ext., etc. Multimodal therapy using Streptococcal phage, **procaine** penicillin, and P24 antigen as well as horse antiserum against **AIDS** were described.

L134 ANSWER 14 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:262222 HCAPLUS
DN 126:272344
TI Antiviral drugs and their enhancers against **HIV**
IN Nakajima, Hideki; Yamada, Kaneo; Igarashi, Toshisato
PA Samu Kenkyusho Kk, Japan
SO Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09059178	A2	19970304	JP 1995-240947	19950824

GI

SOD[C(O)(CH2)nC(O)X]m I

AB Antiviral **formulations** contain lecithin-binding human Cu, **Zn**-SOD (I; X = lyso-lecithin with 2-hydroxy at glycerol; m >1; n >2), **HIV reverse transcriptase** inhibitors (**AZT**, **ddC**, and ddI), **HIV protease** inhibitors (e.g. KNI-272), and/or sulfated polysaccharides (e.g. dextran sulfate). Thus, I was prepd. from human-derived SOD and 2-(4-hydroxycarbonylbytyloyl)lyso-lecithin, and antiviral injections contg. I and other antiviral agents were **formulated**. I in **combination** with **AZT**, **ddC**, ddI, KNI-272, or dextran sulfate had **synergistic** antiviral actions against **HIV**.

IT **9068-38-6**, **Reverse transcriptase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibitors; antiviral drugs and their enhancers against **HIV**)

L134 ANSWER 15 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:249385 HCAPLUS
DN 126:297763
TI Characterization of metal-ion-nucleotide based particulate matter in solutions of 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA)
AU Yuan, Lung-Chi; Visor, Gary C.
CS Dep. of Formulation and Process Development, Gilead Sciences, Incorporated, Foster City, CA, 94404, USA
SO PDA J. Pharm. Sci. Technol. (1997), 51(1), 30-35

CODEN: JPHTEU; ISSN: 1076-397X
PB PDA, Inc.
DT Journal
LA English
AB The antiviral drug 2-[2-(phosphonomethoxy)ethyl]adenine, PMEA, was developed as an i.v. product for the treatment of **human immunodeficiency** virus infection. During the course of stability monitoring, PMEA I.V. injection was found to undergo particulate matter formation under extended storage at ambient temp. Isolation and characterization of the particulates revealed them to be metal ion-PMEA complexes. The principle metal ions assocd. with the particulates were iron and **zinc**, present as trace impurities (.ltoreq. 40 ppm) in PMEA drug substance detd. by inductively coupled argon plasma spectroscopy. These visible particles are characterized by energy-dispersive x-ray spectrometry and fourier transform IR spectroscopy. This study describes the systematic evaluation of the obsd. soln. phenomena and details alternative **formulation** systems to eliminate particulate formation in the PMEA injectable product.
IT **7440-66-6**, **Zinc**, analysis
RL: ANT (Analyte); ANST (Analytical study)
(detn. of iron and **zinc** in **adefovir** injections by inductively coupled argon plasma spectroscopy)

L134 ANSWER 16 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:98389 HCAPLUS
DN 126:194888
TI SRR-SB3, a disulfide-containing macrolide that inhibits a late stage of the replicative cycle of **human immunodeficiency** virus
AU Witvrouw, M.; Balzarini, J.; Pannecouque, C.; Jhaumeer-Laulloo, S.; Este, J. A.; Schols, D.; Cherepanov, P.; Schmit, J.-C.; Debyser, Z.; Vandamme, A.-M.; Desmyter, J.; Ramadas, S. R.; De Clercq, E.
CS Rega Inst. Med. Res., Katholieke Univ. Leuven, Louvain, B-3000, Belg.
SO Antimicrob. Agents Chemother. (1997), 41(2), 262-268
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB From a series of macrocyclin diamides possessing the disulfide linkage, only SRR-SB3, a compd. that complexes with **zinc**, was found to inhibit **human immunodeficiency** virus type 1 (**HIV**-1; strain IIIB) replication at a concn. of 1.8 to 6.5 .mu.g/mL in MT-4, CEM, and peripheral blood mononuclear cells. SRR-SB3 was toxic to MT-4 cells at a concn. of 15.9 .mu.g/mL, resulting in a selectivity index of 9 in these cells. This macrolide was also effective against various other **HIV**-1 strains, including clin. isolates and **HIV**-1 strains resistant to **protease** inhibitors and nucleoside and nonnucleoside **reverse transcriptase** inhibitors. It was also active against various **HIV**-2 strains, simian immunodeficiency virus (strain MAC251), and Moloney murine sarcoma virus, but not against viruses other than retroviruses. In addn., the compd. was found to inhibit chronic **HIV**-1 infections in vitro. The compd. in **combination** with other antiviral agents, such as zidovudine, **zalcitabine**, and stavudine, showed an effect that was between additive and **synergistic**. Time-of-addn. expts. indicated that SRR-SB3 acts at a late stage of the **HIV**-1 replicative cycle.

L134 ANSWER 17 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1997:3179 HCAPLUS

DN 126:108827
TI Formulation and characterization of azidothymidine-loaded liposomes
AU Ravivarapu, Harish; White, Cahterine A.
CS Dep. Pharmaceutics, Univ. Georgia, Athens, GA, 30602, USA
SO Drug Delivery (1996), 3(4), 223-229
CODEN: DDELEB; ISSN: 1071-7544
PB Taylor & Francis
DT Journal
LA English
AB Entrapment efficiency (EE%) and in vitro stability of azidothymidine (**AZT**)-loaded hand-shaken multilamellar vesicles (MLVs), freeze and thaw vesicles (FATMLVs), and reverse phase evapn. vesicles (REVs) were compared. **AZT** entrapment in FATMLVs was further studied by varying initial lipid concns., drug concn., and lipid compn. The results suggest that **AZT** entrapment is dependent on the aq. vol. entrapped within liposomes, and the interaction between the drug and liposomal bilayer may not be significant. Increasing the lipid concn. increases the liposomal entrapment of **AZT** but the encapsulation yield decreases above a lipid concn. of 30 .mu.mol/mL. No significant difference was obsd. in EE% when the **AZT** concn. was varied from 5 to mg/mL. The entrapment efficiency was highest (43.2%) for DSPC/CHOL/PS (molar ratio 6:3:3) vesicles but DSPC/CHOL/PS liposomes formulations in a molar ratio of 4:3:3 or 4:5:1 and DSPC/CHOL/SA liposome formulations in a molar ratio of 4:5:1 were more stable in vitro. In vitro drug release from liposomes was dependent on bilayer compn. and the method of prepn.

L134 ANSWER 18 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1996:596349 HCAPLUS
DN 125:237726
TI The protective role of **zinc** and N-acetylcysteine in modulating zidovudine-induced hematopoietic toxicity
AU Gogu, Sudhir R.; Agrawal, Krishna C.
CS Dep. Pharmacol., Tulane Univ. Sch. Med., New Orleans, LA, 70112, USA
SO Life Sci. (1996), 59(16), 1323-1329
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
AB The role of Zn2+ and N-acetylcysteine (NAC) in protecting hematopoietic progenitor cells from zidovudine (**AZT**)-induced toxicity was studied.. Murine bone **marrow** progenitor cells (BMPC) were exposed to various concns. (0.1-50 .mu.M) of **AZT** in the presence and absence of **Zn**(OAc)2 (100 .mu.M) or NAC (100 .mu.M). The cell survival was detd. by colony-forming assays of erythroid (CFU-E) and granulocytic (CFU-GM) lineage. The IC50 values of **AZT** in the presence of Zn2+ were increased approx. 3-fold (from 3.0 to 9.5 .mu.M) in the CFU-E assay and 7-fold (from 4.3 to 28.8 .mu.M) in the CFU-GM assay, whereas in the presence of NAC, the IC50 values were increased by 2- and 4-fold, resp. To delineate the mechanism of the protection of BMPC by Zn2+, the levels of metallothionein (MT) mRNA were monitored by using a 31-mer cDNA probe. Zn2+ produced a concn.-dependent increase in MT mRNA in BMPC. These results suggest that dietary Zn2+ and NAC supplementation can be used to reduce **AZT**-induced bone **marrow** toxicity.
IT **7440-66-6**, **Zinc**, biological studies
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(zidovudine-induced hematopoietic toxicity inhibition by)

L134 ANSWER 19 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1996:535077 HCAPLUS
DN 125:230787
TI Covalent microparticle-drug conjugates for biological targeting
IN Yatvin, Milton B.; Stowell, Michael H. B.; Gallicchio, Vincent S.; Meredith, Michael J.
PA Oregon Health Sciences University, USA
SO U.S., 29 pp. Cont.-in-part of U.S. Ser. No. 142, 771.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5543390	A	19960806	US 1994-246941	19940519
	US 5149794	A	19920922	US 1990-607982	19901101
	US 5256641	A	19931026	US 1992-911209	19920709
	US 5543389	A	19960806	US 1993-142771	19931026
	US 5543391	A	19960806	US 1995-441770	19950516
	WO 9532002	A1	19951130	WO 1995-US6180	19950517
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9526393	A1	19951218	AU 1995-26393	19950517
	EP 759784	A1	19970305	EP 1995-921275	19950517
	R: BE, CH, DE, FR, GB, LI, NL, SE				
	US 5840674	A	19981124	US 1996-691891	19960801

PRAI US 1990-607982 19901101
US 1992-911209 19920709
US 1993-142771 19931026
US 1994-246941 19940519
US 1995-441770 19950516
WO 1995-US6180 19950517

AB This invention provides novel methods and reagents for specifically delivering biol. active compds. to phagocytic mammalian cells. The invention also relates to specific uptake of such biol. active compds. by phagocytic cells and delivery of such compds. to specific sites intracellularly. The invention specifically relates to methods of facilitating the entry of antimicrobial drugs and other agents into phagocytic cells and for targeting such compds. to specific organelles within the cell. The invention specifically provides **compns**. of matter and pharmaceutical embodiments of such **compns**. comprising conjugates of such antimicrobial drugs and agents covalently linked to particulate carriers generally termed microparticles. In particular embodiments, the antimicrobial drug is covalently linked to a microparticle via an org. linker mol. which is the target of a microorganism-specific protein having enzymic activity. Thus, the invention provides cell targeting of drugs wherein the targeted drug is only released in cells infected with a particular microorganism. Alternative embodiments of such specific drug delivery **compns**. also contain polar lipid carrier mols. effective in achieving intracellular organelle targeting in infected phagocytic mammalian cells. Particular embodiments of such conjugates comprise antimicrobial drugs covalently linked both to a microparticle via an org. linker mol. and to a polar lipid compd., to facilitate targeting of such drugs to particular

subcellular organelles within the cell. Also provided are porous microparticles impregnated with antimicrobial drugs and agents wherein the surface or outside extent of the microparticle is covered with a degradable coating that is specifically degraded within an infected phagocytic mammalian cell. Methods of inhibiting, attenuating, arresting, combating and overcoming microbial infection of phagocytic mammalian cells in vivo and in vitro are also provided.

L134 ANSWER 20 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1996:422386 HCAPLUS
DN 125:76341
TI A method for identifying and using compounds that inactivate HIV-1 and other retroviruses by attacking highly conserved **zinc** fingers in the viral nucleocapsid protein
IN Henderson, Louis E.; Arthur, Larry O.; Rice, William G.
PA United States Dept. of Health and Human Services, USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9609406	A1	19960328	WO 1995-US11915	19950919
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9535927	A1	19960409	AU 1995-35927	19950919
EP 782632	A1	19970709	EP 1995-933161	19950919
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

PRAI US 1994-312331 19940923
WO 1995-US11915 19950919
OS MARPAT 125:76341
AB Several classes of compds. (disulfides, maleimides, .alpha.-halogenated ketones, hydrazides, nitric oxide and NO-contg. derivs., cupric ions and complexes thereof, ferric ions and complexes thereof) are provided which can be used to inactivate retroviruses, e.g. HIV-1, by attacking the CCHC **zinc** fingers of the viral nucleocapsid protein and ejecting the **zinc** therefrom. In addn., kits for identifying compds. that can react with CCHC **zinc** fingers of the nucleocapsid proteins of a large no. of different retroviruses have also been developed. The kits of the present invention describe a set of specific tests and reagents that can be used to screen and identify compds. based on their ability to react with and disrupt retroviral **zinc** fingers in the viral NC proteins and, in turn, inactivate the retrovirus of interest. The effect of e.g. disulfides on HIV-1 is included.
IT **7440-66-6, Zinc**, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(identification and use of compds. inactivating HIV-1 and other retroviruses by attacking highly conserved **zinc** fingers in viral nucleocapsid protein)

L134 ANSWER 21 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1996:311690 HCAPLUS
DN 124:333050

TI Improved anti-infective polyoxypropylene/polyoxyethylene copolymers and methods of use
IN Emanuele, R. Martin; Balasubramanian, Mannarsamy; Allaudeen, Hameedsulthan S.
PA Cytrx Corporation, USA
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9604924	A1	19960222	WO 1995-US9637	19950809
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5567859	A	19961022	US 1994-292803	19940809
	US 5674911	A	19971007	US 1995-468137	19950606
	AU 9533598	A1	19960307	AU 1995-33598	19950809

PRAI US 1994-292803 19940809
US 1995-468137 19950606
US 1987-17330 19870220
US 1988-141668 19880107
US 1988-150731 19880216
US 1989-419016 19891010
US 1991-673289 19910319
US 1991-760808 19910916
US 1992-847874 19920313
US 1993-81006 19930622
US 1993-87136 19930702
US 1993-161551 19931202
US 1995-457808 19950601
WO 1995-US9637 19950809

AB The present invention comprises novel prepns. of polyoxypropylene/polyoxyethylene copolymers which retain the therapeutic activity of the com. prepns., but substantially reduce the undesirable effects which are inherent in the prior art prepns. Because the prepns. of polyoxypropylene/polyoxyethylene copolymers which comprise the present invention are a less polydisperse population of mols. than the prior art polyoxypropylene/polyoxyethylene copolymers, the biol. activity of the copolymers is better defined and more predictable and the cardiotoxicity inherent in the native copolymers is substantially reduced. In accordance with the present invention, a **compn.** and method are provided that is effective in treating infections caused by microorganisms including, but not limited to, bacteria, viruses, protozoa, and fungi. The present invention is effective in inhibiting the growth of bacteria such as Myocobacterium species including, but not limited to, Mycobacterium avium-intracellular complex and M. tuberculosis.

IT **65277-42-1, Ketoconazole**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(infection treatment with anti-infective polyoxypropylene-polyoxyethylene block copolymer and drugs)

L134 ANSWER 22 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1996:277730 HCAPLUS
DN 124:331807
TI Inhibition of **human immunodeficiency** virus-1 **reverse transcriptase** by heme and synthetic heme analogs
AU Staudinger, Robert; Abraham, Nader G.; Levere, Richard D.; Kappas, Attallah

CS Rockefeller University, New York, NY, 10021-6399, USA
SO Proc. Assoc. Am. Physicians (1996), 108(1), 47-54
CODEN: PAAPFD; ISSN: 1081-650X
DT Journal
LA English
AB Heme and a series of synthetic heme analogs were tested for inhibition of **human immunodeficiency** virus-1 (**HIV**-1) **reverse transcriptase** (RT) activity. Heme and the protoporphyrin complexes of cadmium, magnesium, and tin significantly inhibited **HIV**-1 RT, whereas other metalloporphyrins had a lesser or no effect on the enzyme. The mechanism of inhibition was examd. with respect to heme and tin protoporphyrin (SnPP), as both compds. have been utilized clin. as treatment for noninfectious disorders. Heme and SnPP inhibited **HIV**-1 RT in a noncompetitive manner with respect to deoxythymidine triphosphate. Inhibition depended in part on the protoporphyrin structure, because the meso derivs. of the heme analogs essentially were without effect. Heme also markedly enhanced the inhibitory effect of azidothymidine (zidovudine, **AZT**) on **HIV**-1 RT, and the **combination** of the two compds. showed **synergy** in inhibiting **HIV**-1 RT. **HIV**-1 RT was used to reverse transcribe the glyceraldehyde phosphate dehydrogenase (GAPDH) gene from human kidney. Subsequently, GAPDH cDNA was amplified with Taq polymerase, and electrophoresis showed that **HIV**-1 RT catalyzed the reverse transcription of human mRNA at a rate comparable to that of Moloney murine leukemia virus. Heme and SnPP prevented cDNA synthesis by **HIV**-1 RT in this RT-polymerase chain reaction assay. We also examd. the effects of these compds. on normal human bone **marrow** function. Heme stimulated both erythroid and myeloid progenitor colony formation, whereas SnPP was essentially without effect. In contrast, ZnPP had a suppressive effect on hematopoiesis. Finally, we show that heme has a sparing effect against the myelotoxicity of **AZT**. The results of these studies raise the possibility that **combination** therapy with **AZT** and heme, or heme plus an inhibitor of heme catabolism, might have therapeutic potential in the **acquired immunodeficiency** syndrome.
IT **9068-38-6, Reverse transcriptase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibition of **human immunodeficiency** virus-1 **reverse transcriptase** by heme and synthetic heme analogs)

L134 ANSWER 23 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:924530 HCAPLUS
TI Synthesis of **AZT**-Pt(terpy) -- a potential compound for radiotherapy of **aids**.
AU Mirzadeh, Saed; Packard, Alan B.
CS Nuclear Medicine Group, Oak Ridge National Laboratory, Oak Ridge, TN, 37831-6229, USA
SO Book of Abstracts, 210th ACS National Meeting, Chicago, IL, August 20-24 (1995), Issue Pt. 2, NUCL-009 Publisher: American Chemical Society, Washington, D. C.
CODEN: 61XGAC
DT Conference; Meeting Abstract
LA English
AB The aim of this work is to evaluate a novel approach for the potential control of **AIDS** using radiotherapy. We propose to evaluate the **combined** therapeutic effectiveness of the Auger-electron emitter 195mPt when it is attached to **AZT** and other related nucleoside drugs. Auger electrons penetrate only a short distance in tissue, thus

the radiation dose will be confined to the infected cells only. With this approach, we expect to target not only the infected cells but also the mononuclear macro-phages which engulf the dead cells. It has been shown that chloro(2, 2', 6', 2"-terpyridine)Pt(II)+, Pt(terpy)Cl, is a suitable reagent for modification of proteins by binding to the histidine residues [JACS 109, 4592 (1987)]. Based on these results and those on formation of ternary complexes of **Zn**(II)-cyclen with **AZT** [JACS 115, 6730 (1993)], we expected that in neutral solns., the deprotonated imide nitrogen, on the thymine moiety of **AZT** (pKa = 9.65) would replace the Cl- group of [Pt(terpy)Cl]+. At a 1:1 molar ratio, the above reaction proceeds very slowly with a t1/2 of several days. At 5-fold molar excess of **AZT**, the reaction is completed within 24 h. The **AZT**-Pt(terpy) complex was sepd. from the excess **AZT** on cation exchanger Sephadex-SP using H2O and 0.2 M NaCl as eluent.

L134 ANSWER 24 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1995:566590 HCAPLUS
DN 123:7685
TI Activity of Cu2Zn2 superoxide dismutase against the human immunodeficiency virus type 1
AU Miesel, R.; Mahmood, N.; Weser, U.
CS Deutsches Rheuma Forschungs Zentrum, German Rheumatology Research Center, Berlin, D-13353, Germany
SO Redox Rep. (1995), 1(2), 99-103
CODEN: RDRPE4; ISSN: 1351-0002
DT Journal
LA English
AB The anti-retroviral activity of Cu2Zn2 superoxide dismutase (SOD; EC 1.15.1.1) was tested in Molt-4 cells infected with the human immunodeficiency virus type 1 (HIV-1) and compared to the anti-HIV-1 activity of the **reverse transcriptase** inhibitors azidothymidine (**AZT**), dideoxycytidine (**ddC**), dideoxyuridine (ddU) and phosphonoformic acid, the glucosidase I inhibitors castanospermine and dihydroxymethyl dihydroxy-pyrrolidine (DMDP), the HIV **protease** inhibitor RO-31-7595 as well as the CD4-masking compd. aurintricarboxylic acid. 300 NM of SOD sufficed to reduce the release of the viral antigen gp120 of HIV-1NDK-infected Molt-4 cells by 50% [EC50]. Cytotoxic effects of SOD were estd. by cell counts and rates of cell growth. SOD, 3 .mu.M, reduced the cell growth of uninfected cells by 50% [TC50]. While copper-free apo-SOD displayed no anti-HIV activity, the [EC50] of heat-inactivated enzyme was 1 .mu.M, suggesting an anti-retroviral effect of low mol. wt. active center degrdn. products of SOD. The [EC50] of SOD reached 10% of **AZT**'s anti-HIV-1NDK activity and exceeded all tested anti-retrovirals 40-3000-fold. The selectivity index (Si=[TC50]/[EC50] for SOD was 10, resembling the **reverse transcriptase** inhibitors dideoxycytidine and phosphonoformic acid. SOD inhibited also dose-dependently the oxidative stress induced depletion of sulfhydryls, which are crucially involved in the nuclear factor kappa B controlled HIV transcription.

L134 ANSWER 25 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1994:499130 HCAPLUS
DN 121:99130
TI Amelioration of azidothymidine-induced erythroid toxicity by hemin and stem cell factor in immune-suppressed mice
AU Hamburger, Anne W.; Chen, Rong-Bing
CS Dep. Pathol., Univ. Md. Cancer Cent., Baltimore, MD, 21201, USA
SO Exp. Hematol. (Charlottesville, Va.) (1994), 22(4), 348-52

CODEN: EXHMA6; ISSN: 0301-472X
DT Journal
LA English
AB Recombinant cytokines such as stem cell factor (SCF) are currently being tested for the ability to ameliorate 3'azido-3'deoxythymidine (**AZT**)-induced **anemia** in **AIDS** patients. Recently, the authors showed that SCF greatly increased burst-forming units-erythroid (BFU-E) but failed to increase hematocrits of **AZT**-treated **immune-deficient** (MAIDS) mice. The authors reasoned that hemin, previously shown to both enhance BFU-E proliferation and accelerate erythroid maturation, might bring about differentiation of this large SCF-induced pool of BFU-E and further protect BFU-E from **AZT**'s toxic effect. The authors therefore studied, in vitro, the effect of **combinations** of hemin and SCF on growth of BFU-E from MAIDS mice. Hemin, at concns. of 10 to 100 .mu.M, ameliorated the growth-inhibitory effect of **AZT**. 50 .mu.M hemin increased the ED50 of **AZT** from 1.times.10-7M to 1.7.times.10-6M. SCF also ameliorated **AZT**-induced toxicity, but to a lesser extent. SCF and hemin increased the no. of BFU-E colonies obsd. in the presence of **AZT** in an additive fashion. The resistance of BFU-E to **AZT**'s cytotoxic effect was greater in cultures receiving hemin and SCF together than in cultures receiving SCF or hemin alone. **Zinc** and tin protoporphyrins (**Zn** and Sn PP) increased the nos. of BFU-E obsd. However, neither **zinc** nor tin protoporphyrins increased the ED50 of **AZT**. **Combinations** of SCF and hemin may prove useful in ameliorating **AZT** toxicity in both **immune**-suppressed mice and **human immunodeficiency** virus (**HIV**)-infected patients.

L134 ANSWER 26 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1994:474117 HCAPLUS
DN 121:74117
TI inhibition of 3'-azido-3'-deoxythymidine-resistant **HIV**-1 infection by **dehydroepiandrosterone** in vitro
AU Yang, Jyh-Yuan; Schwartz, Arthur; Henderson, Earl E.
CS Sch. Med., Temple Univ., Philadelphia, PA, 19140, USA
SO Biochem. Biophys. Res. Commun. (1994), 201(3), 1424-32
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB **Human immunodeficiency** virus type 1 (**HIV**-1) isolated from patients with **acquired immunodeficiency** syndrome (**AIDS**) shows resistance to 3' azido-3' deoxythymidine (**AZT**) after one or two years of treatment. The authors investigated whether **DHEA** treatment could inhibit replication of **AZT**-resistant strains of **HIV**-1. Addn. of **DHEA** to MT-2 cell cultures infected with either **AZT**-sensitive or **AZT**-resistant isolates of **HIV**-1 resulted in dose-dependent inhibition of **HIV**-1-induced cytopathic effect and suppression of **HIV**-1 replication as measured by accumulation of **reverse transcriptase** activity. At a concn. as low as 50 .mu.M, **DHEA** reduced **AZT**-resistant **HIV**-1 replication over 50% as measured by cytopathic effect and accumulation of **reverse transcriptase** activity. This study provides evidence that **DHEA** can inhibit the replication of **AZT**-resistant as well as wild-type **HIV**-1. Since the main target for **DHEA** are metabolic and cellular signaling pathways leading to **HIV**-1 replication-activation, **DHEA** should be effective against multidrug-resistant strains of **HIV**-1.

Combined with recently discovered immunoregulatory properties, the finding that **DHEA** is able to inhibit replication of both wild-type and **AZT**-resistant **HIV**-1 suggests that in vivo **DHEA** may have a much broader spectrum of action than originally anticipated.

IT **53-43-0, Dehydroepiandrosterone**
RL: BIOL (Biological study)
(**AZT**-resistant **HIV**-1 replication inhibition by)

L134 ANSWER 27 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1994:200438 HCAPLUS
DN 120:200438
TI Controlled-release transdermal pharmaceuticals containing cyrogels
IN Wood, Louis L.; Calton, Gary J.
PA SRCHEM Inc., USA
SO U.S., 15 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5260066	A	19931109	US 1992-821627	19920116
	US 5288503	A	19940222	US 1992-899369	19920616
PRAI	US 1992-821627		19920116		

AB A controlled-release transdermal pharmaceutical contg. therapeutic agents in a poly(vinyl alc.) (I) cyrogel is disclosed. A slurry of 11.0 mg ciprofloxacin.HCl (II) and 200 mg 10% I was warmed to 50-60.degree. to obtain a clear homogeneous soln. The soln. was then placed in a mold and subjected to 6 freeze-thaw cycles to give a white opaque elastomeric cryogel having 15mm diam. and 0.5mm thickness. The release of II from the gel in 0.9% NaCl was 74% in th 1st 4 hs and it was const. in the subsequent 5-24 hs.

IT **50-81-7, Vitamin C**, biological studies
51-05-8, Procaine hydrochloride **57-41-0, Phenytoin 59-46-1, Procaine 137-58-6, Lidocaine 4205-90-7, Clonidine 7440-66-6D, Zinc**, salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release transdermal pharmaceuticals contg. cryogels and)

L134 ANSWER 28 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1993:440940 HCAPLUS
DN 119:40940
TI Uses of acemannan or other aloe products in the treatment of diseases requiring intervention of the immune system for cure
IN McAnalley, Bill H.; Carpenter, Robert H.; McDaniel, Harley R.
PA Carrington Laboratories, Inc., USA
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9308810	A1	19930513	WO 1991-US8204	19911105
	W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE, BF, BJ, CF,				

CG, CI, CM, GA, GN, ML, MR, SN, TD, TG

AU 9190831	A1	19930607	AU 1991-90831	19911105
EP 611304	A1	19940824	EP 1992-900586	19911105
R: DE, FR, GB, IT				

PRAI WO 1991-US8204 19911105

AB Acemannan (I) is effective in treating a no. of conditions where the principal mechanism of resoln. or cure requires intervention by the patient's immune system. I has direct stimulatory effects on the immune system. Methods for treating cancer, viral diseases, respiratory and immune regulatory diseass, inflammation, and infections and infestations by administering an acetylated mannan deriv., e.g. I derived from aloe, are described. The method finds use in tissue cultures, animals, and plants. A large variety of case studies describing the effectiveness of I in the treatment of a variety of conditions are presented.

IT **65277-42-1**
RL: BIOL (Biological study)
(human immunodeficiency virus-assocd. fungal infection treatment with acemannan and)

L134 ANSWER 29 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1993:87649 HCAPLUS
DN 118:87649
TI Glutathione-containing immunostimulant dietary supplement
IN Khaled, F. Mahnaz
PA Life Sciences Technologies, Inc., USA
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9221368	A1	19921210	WO 1992-US4653	19920604
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9221879	A1	19930108	AU 1992-21879	19920604
EP 604433	A1	19940706	EP 1992-913917	19920604
R: DE, FR, GB				

PRAI US 1991-711530 19910606
WO 1992-US4653 19920604

AB A nutrient **compn.** for the treatment of immune disorders comprises oxidized or nonoxidized glutathione, or its equiv., in **combination** with glutamine, vitamins and Se. A **compn.** contained glutathione 250, L-glutamine, .beta.-carotene 15, L-arginine 75, Fe 10, Mg 20, riboflavin 10, thiamine 10, vitamin A 4, vitamin B6 8, **vitamin C** 500, vitamin E 150, **Zn** 15 mg, and Cr 15, folic acid 100, Se 25, and vitamin B12 1.0 .mu.g. The **compn** . enhanced the in vitro survival of T4 lymphocytes (CEM cell line) infected with the **human immunodeficiency** virus-1, in the presence of **AZT**, as shown by the method of Wieslow and al. (1989). With **AZT** alone, cell growth inhibition was noted, thus indicating toxicity.

IT **50-81-7, Vitamin C**, biological studies
7440-66-6, Zinc, biological studies
RL: BIOL (Biological study)
(nutritional supplement contg., for treatment of immune disorders)

L134 ANSWER 30 OF 33 HCAPLUS COPYRIGHT 1999 ACS

AN 1992:639842 HCAPLUS
DN 117:239842
TI Transdermal compositions containing high concentration of active agents
IN Taylor, Reginald Morton; Wilson, David John
PA Commonwealth Scientific and Industrial Research Organization, Australia
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9214442	A1	19920903	WO 1992-AU58	19920218
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
	RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
	US 5308621	A	19940503	US 1991-795499	19911121
	CA 2103725	AA	19920819	CA 1992-2103725	19920218
	AU 9212723	A1	19920915	AU 1992-12723	19920218
	AU 668679	B2	19960516		
	EP 572494	A1	19931208	EP 1992-905485	19920218
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL				
	JP 06508100	T2	19940914	JP 1992-504787	19920218
PRAI	AU 1991-4651	19910218			
	AU 1991-7846	19910819			
	AU 1991-7847	19910819			
	AU 1991-7848	19910819			
	US 1991-795499	19911121			
	WO 1992-AU58	19920218			

AB The title compn. comprises a biol. active agent at a concn. above its soly. limit in a carrier at ambient conditions, wherein there are sufficient fine particles of the agent dispersed through the carrier to facilitate the transdermal transfer capacity of the compn. For example, a compn. contg. ibuprofen (I), glycerol 26.2, propylene glycol 21.6, and polyethylene glycol 2.5g was prepd. The particle size of I in the compn. was much smaller than that of I in a com. available cream.
IT **50-81-7**, L-**Ascorbic acid**, biological studies
4205-90-7
RL: BIOL (Biological study)
(transdermal compns. contg.)

L134 ANSWER 31 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1992:503623 HCAPLUS
DN 117:103623
TI 3'-Azido-3'-deoxythymidine drug interactions. Screening for inhibitors in human liver microsomes
AU Rajaonarison, Jean Francois; Lacarelle, Bruno; Catalin, Jacques; Placidi, Michel; Rahmani, Roger
CS Lab. Toxicocinet. Pharmacocinet., Fac. Pharm., Marseille, 13385, Fr.
SO Drug Metab. Dispos. (1992), 20(4), 578-84
CODEN: DMDSAI; ISSN: 0090-9556
DT Journal
LA English
AB Zidovudine is a widely used antiretroviral drug active against **human immunodeficiency** virus. The drug interactions of this compd., which are primarily eliminated as a glucuronide, have not yet been extensively studied. Because zidovudine is frequently **combined** with other drugs, complete knowledge of interactions is

essential to optimize **AIDS** therapy. The authors therefore screened the effect of 55 mols., representative of 20 different therapeutic classes, on 3'-azido-3'-deoxythmidine (**AZT**) glucuronidation by human liver microsomes. Many drugs caused more than 15% inhibition of **AZT** glucuronidation in vitro, whereas major antibiotics (ceftazidime, isoniazid, aminoglycosides, macrolides, and sulfamides), antivirals (2',3'-dideoxycytidine, 2',3'-dideoxyinosine, and acyclovir), flucytosine, metronidazole, acetaminophen, and ranitidine had no effect. For compds. that appeared to inhibit **AZT** glucuronidation, extrapolation to the clin. situation must take into account both the in vitro apparent Ki values and the usual expected plasma level for the coadministered drug. By considering these parameters, this work indicates that clin. relevant inhibition for **AZT** glucuronidation may be obsd. with the following drugs: cefoperazone, penicillin G, amoxicillin, piperacillin, chloramphenicol, vancomycin, miconazole, rifampicin, phenobarbital, carbamazepine, **phenytoin**, valproic acid, quinidine, phenylbutazone, ketoprofen, probenecid, and propofol. Complementary clin. and pharmacokinetic studies should be performed to validate these assumptions.

IT **57-41-0, Phenytoin**
RL: BIOL (Biological study)
(azidodeoxythymidine glucuronidation inhibition by, in human liver microsomes)

L134 ANSWER 32 OF 33 HCAPLUS COPYRIGHT 1999 ACS
AN 1990:125194 HCAPLUS
DN 112:125194
TI Liposomal nucleoside analogs for treating AIDS
IN Hostetler, Karl Y.; Richman, Douglas D.
PA University of California, USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8902733	A1	19890406	WO 1988-US3210	19880919
	W: AU, JP				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8825261	A1	19890418	AU 1988-25261	19880919
	EP 380558	A1	19900808	EP 1988-908811	19880919
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 03501253	T2	19910322	JP 1988-508005	19880919
PRAI	US 1987-99755		19870922		
	WO 1988-US3210		19880919		

AB Phosphorylated nucleoside analogs are encapsulated in liposomes for use in treating AIDS and related retroviral infections. The nucleoside analogs are selected from the group consisting of azidothymidine, dideoxycytidine, dideoxyadenosine, and ribavirin and phosphorylated before the encapsulation to prevent leakage, resulting in reduced toxic side effects and enhanced inhibition of replication of HIV or related viruses present in monocytes and macrophages. 3H-labeled **AZT**-5'-monophosphate (I) was encapsulated in phosphatidylcholine/**cholesterol** liposomes; retention rate of I was higher than that of 3H-**AZT**. Effects of liposomes contg. I on HIV-infected MT-2 cells, U937 cells, and human macrophages are detailed.

L134 ANSWER 33 OF 33 HCAPLUS COPYRIGHT 1999 ACS

AN 1985:202026 HCAPLUS
DN 102:202026
TI Mechanism of action of diabetogenic **zinc**-chelating agents. Model system studies
AU Epand, R. M.; Stafford, A. R.; Tyers, M.; Nieboer, E.
CS Dep. Biochem., McMaster Univ., Hamilton, ON, L8N 3Z5, Can.
SO Mol. Pharmacol. (1985), 27(3), 366-74
CODEN: MOPMA3; ISSN: 0026-895X
DT Journal
LA English
AB Using model systems, the authors studied the properties of a no. of **Zn**-chelating agents which are known to cause diabetes in lab. animals. The abilities to permeate membranes and to complex **Zn** inside liposomes with the release of protons are suggested as chem. properties that can enhance diabetogenicity. When such complexing agents are added to lipid vesicles at pH 6 contg. entrapped Zn2+, they acidify the contents of these vesicles. The authors demonstrated this effect by measuring intravesicular pH both with a F-contg. F NMR probe as well as with the fluorescent probe, quinine. Using quinine, it was obsd. that 0.1 mM 8-hydroxyquinoline reduced the intravesicular pH of sonicated phospholipid vesicles contg. entrapped Zn2+ (as sulfate) from pH 6.0 to 2.8. These diabetogenic chelating agents also solubilized **Zn-insulin** ppts. from unbuffered suspensions at pH 6.0. The solubilization results from the acidification of these suspensions. Dithizone and 8-hydroxyquinoline at 4 mM solubilized 97 and 42%, resp., of the suspended **insulin**. It is suggested that if such proton release occurs within the **Zn**-contg. **insulin** storage granules of pancreatic .beta.-cells, solubilization of **insulin** would be induced. Such an event would lead to osmotic stress and eventually to rupture of the granule. The effects of diethyldithiocarbamate (**DDC**), an agent that protects rabbits against the induction of diabetes by some other **Zn**-chelating agents, were also studied. **DDC** caused a decrease of 3.5 units in the intravesicular pH of **Zn**-contg. vesicles by a mechanism not involving the release of protons upon chelation of **Zn**. Several properties of **DDC** which may contribute to its ability to protect against the induction of diabetes were demonstrated. These include its ability to store **Zn** as a hydrophobic complex in membranes, its consumption of protons upon spontaneous decompn., and the ability of one of its decompn. products, diethylamine, to accelerate the dissipation of pH gradients across lipid bilayers. Diethylamine is particularly effective in stimulating a rapid dissipation of such pH gradients, even at micromolar concns. The authors attempted to est. quant. the extent of proton liberation by various **Zn**-chelating agents. This anal. demonstrated that partitioning of the ligand between org. and aq. phases, ligand acidity, and **Zn** complex stability det. the extent of proton release.
IT **7440-66-6**, biological studies
RL: BIOL (Biological study)
(chelating agents for, diabetes from, mechanisms in)

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E9 THROUGH E18 ASSIGNED

=> fil reg
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STRUCTURE FILE UPDATES: 24 JUL 99 HIGHEST RN 228878-07-7
DICTIONARY FILE UPDATES: 24 JUL 99 HIGHEST RN 228878-07-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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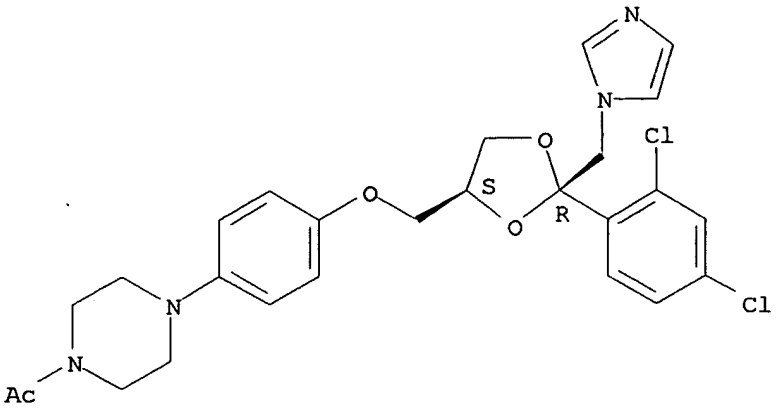
1 7440-66-6/BI
(7440-66-6/RN)
1 65277-42-1/BI
(65277-42-1/RN)
1 50-81-7/BI
(50-81-7/RN)
1 57-41-0/BI
(57-41-0/RN)
1 9068-38-6/BI
(9068-38-6/RN)
1 4205-90-7/BI
(4205-90-7/RN)
1 137-58-6/BI
(137-58-6/RN)
1 51-05-8/BI
(51-05-8/RN)
1 53-43-0/BI
(53-43-0/RN)
1 59-46-1/BI
(59-46-1/RN)
L146 10 (7440-66-6/BI OR 65277-42-1/BI OR 50-81-7/BI OR 57-41-0/BI OR 9068-38-6/BI OR 4205-90-7/BI OR 137-58-6/BI OR 51-05-8/BI OR 53-43-0/BI OR 59-46-1/BI)

=> d ide can tot

L146 ANSWER 1 OF 10 REGISTRY COPYRIGHT 1999 ACS
RN **65277-42-1** REGISTRY
CN Piperazine, 1-acetyl-4-[4-[[(2R,4S)-2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-, rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Piperazine, 1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-, cis-
OTHER NAMES:
CN (.+-.)-Ketoconazole
CN Ketoconazole
CN Nizoral
CN R 41400
FS STEREOSEARCH
DR 72093-26-6
MF C26 H28 Cl2 N4 O4
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAPLUS, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CIN, CSCHEM, CSNB, DDFU, DRUGPAT, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Relative stereochemistry.



1582 REFERENCES IN FILE CA (1967 TO DATE)
28 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1584 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:63203

REFERENCE 2: 131:55184

REFERENCE 3: 131:53527

REFERENCE 4: 131:49461

REFERENCE 5: 131:49197

REFERENCE 6: 131:29714

REFERENCE 7: 131:27500

REFERENCE 8: 131:27423

REFERENCE 9: 131:16303

REFERENCE 10: 131:13987

L146 ANSWER 2 OF 10 REGISTRY COPYRIGHT 1999 ACS
RN **9068-38-6** REGISTRY
CN Nucleotidyltransferase, deoxyribonucleate, RNA-dependent (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Reverse transcriptase
CN Revertase
CN RNA revertase
CN RNA-dependent deoxyribonucleate nucleotidyltransferase
CN RNA-dependent DNA polymerase
CN RNA-directed DNA polymerase

CN RNA-instructed DNA polymerase
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, CA, CABA, CAPLUS, CEN, CHEMCATS, CHEMLIST, CBNB, CIN, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, NAPRALERT, PIRA, PROMT, TOXLINE, TOXLIT, USPATFULL
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
5192 REFERENCES IN FILE CA (1967 TO DATE)
59 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5201 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:57512

REFERENCE 2: 131:56719

REFERENCE 3: 131:55747

REFERENCE 4: 131:54755

REFERENCE 5: 131:54734

REFERENCE 6: 131:53641

REFERENCE 7: 131:53624

REFERENCE 8: 131:53618

REFERENCE 9: 131:53584

REFERENCE 10: 131:53571

L146 ANSWER 3 OF 10 REGISTRY COPYRIGHT 1999 ACS
RN **7440-66-6** REGISTRY
CN Zinc (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Asarco L 15
CN Blue powder
CN Ecka 4
CN F 1000
CN F 1000 (metal)
CN F 1500T
CN F 2000
CN F 2000 (metal)
CN LS 2
CN LS 2 (element)
CN LS 4
CN LS 5
CN LS 5 (metal)
CN NC-Zinc
CN Rheinzink
CN UF
CN UF (metal)
CN VM 4P16
DR 12793-53-2, 195161-85-4, 199281-21-5
MF Zn
CI COM

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, APILIT, APILIT2, APIPAT, APIPAT2, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CHEMSAFE, CIN, CSCHEM, CSNB, DETHERM*, DDFU, DIPPR*, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA, ULIDAT, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Zn

181783 REFERENCES IN FILE CA (1967 TO DATE)
9568 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
181895 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:67336

REFERENCE 2: 131:67331

REFERENCE 3: 131:67328

REFERENCE 4: 131:67280

REFERENCE 5: 131:67278

REFERENCE 6: 131:67268

REFERENCE 7: 131:67263

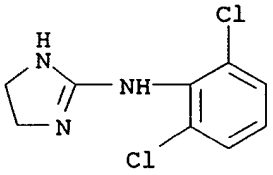
REFERENCE 8: 131:66996

REFERENCE 9: 131:66689

REFERENCE 10: 131:66476

L146 ANSWER 4 OF 10 REGISTRY COPYRIGHT 1999 ACS
RN **4205-90-7** REGISTRY
CN 1H-Imidazol-2-amine, N-(2,6-dichlorophenyl)-4,5-dihydro- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Imidazoline, 2-(2,6-dichloroanilino)- (7CI, 8CI)
OTHER NAMES:
CN 2-(2,6-Dichloroanilino)-2-imidazoline
CN 2-(2,6-Dichlorophenylimino)imidazolidine
CN 734571A
CN Clonidin
CN Clonidine
CN M 5041T
CN SKF 34427
FS 3D CONCORD
DR 57066-25-8, 138474-59-6
MF C9 H9 Cl2 N3
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,

CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CBNB, CIN, CSCHEM, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



5319 REFERENCES IN FILE CA (1967 TO DATE)
50 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
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3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:63477

REFERENCE 2: 131:53959

REFERENCE 3: 131:53947

REFERENCE 4: 131:53868

REFERENCE 5: 131:53787

REFERENCE 6: 131:40048

REFERENCE 7: 131:39641

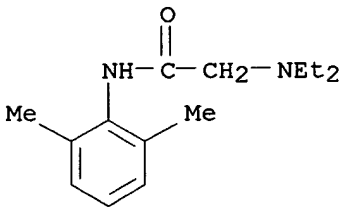
REFERENCE 8: 131:39633

REFERENCE 9: 131:39632

REFERENCE 10: 131:39585

L146 ANSWER 5 OF 10 REGISTRY COPYRIGHT 1999 ACS
RN **137-58-6** REGISTRY
CN Acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2',6'-Acetoxylidide, 2-(diethylamino)- (8CI)
OTHER NAMES:
CN .alpha.-Diethylamino-2,6-acetoxylidide
CN 2-(Diethylamino)-2',6'-acetoxylidide
CN Anbesol
CN Anestacon
CN Duncaine
CN Isicaina
CN Isicaine
CN Leostesin
CN Lidocaine

CN Lignocaine
CN Maricaine
CN Medicaine
CN Remicaine
CN Rucaina
CN Solcain
CN Xilina
CN Xycaine
CN Xylestesin
CN Xyline
CN Xylocain
CN Xylocaine
CN Xylocitin
FS 3D CONCORD
DR 8059-42-5, 8059-66-3, 91484-71-8
MF C14 H22 N2 O
CI COM
LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CBNB, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



5284 REFERENCES IN FILE CA (1967 TO DATE)
60 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5288 REFERENCES IN FILE CAPLUS (1967 TO DATE)
31 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:57355

REFERENCE 2: 131:53860

REFERENCE 3: 131:53599

REFERENCE 4: 131:49343

REFERENCE 5: 131:39648

REFERENCE 6: 131:39641

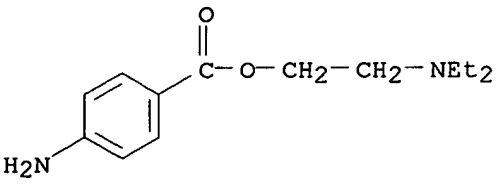
REFERENCE 7: 131:39571

REFERENCE 8: 131:39545

REFERENCE 9: 131:39442

REFERENCE 10: 131:39185

L146 ANSWER 6 OF 10 REGISTRY COPYRIGHT 1999 ACS
RN **59-46-1** REGISTRY
CN Benzoic acid, 4-amino-, 2-(diethylamino)ethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzoic acid, p-amino-, 2-(diethylamino)ethyl ester (8CI)
OTHER NAMES:
CN .beta.-(Diethylamino)ethyl p-aminobenzoate
CN .beta.-Diethylaminoethyl 4-aminobenzoate
CN 2-(Diethylamino)ethyl p-aminobenzoate
CN 2-Diethylaminoethyl 4-aminobenzoate
CN 4-Aminobenzoic acid 2-(diethylamino)ethyl ester
CN 4-Aminobenzoic acid diethylaminoethyl ester
CN Diethylaminoethyl p-aminobenzoate
CN Duracaine
CN Nissocaine
CN p-Aminobenzoic acid 2-diethylaminoethyl ester
CN Procain
CN Procaine
CN Procaine base
CN Spinocaine
CN Vitamin H3
FS 3D CONCORD
DR 91484-72-9
MF C13 H20 N2 O2
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DETHERM*, DDFU, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



2149 REFERENCES IN FILE CA (1967 TO DATE)
35 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2149 REFERENCES IN FILE CAPLUS (1967 TO DATE)
58 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:28213

REFERENCE 2: 131:27803

REFERENCE 3: 131:14954

REFERENCE 4: 131:13852

REFERENCE 5: 131:13848

REFERENCE 6: 131:13766

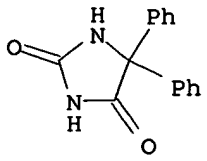
REFERENCE 7: 130:359083

REFERENCE 8: 130:335811

REFERENCE 9: 130:332708

REFERENCE 10: 130:332707

L146 ANSWER 7 OF 10 REGISTRY COPYRIGHT 1999 ACS
RN **57-41-0** REGISTRY
CN 2,4-Imidazolidinedione, 5,5-diphenyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Hydantoin, 5,5-diphenyl- (8CI)
OTHER NAMES:
CN 5,5-Diphenyl-2,4-imidazolidinedione
CN 5,5-Diphenylhydantoin
CN Aleviatin
CN Denyl
CN Di-Hydan
CN Di-Lan
CN Dihycon
CN Dilabid
CN Dintoina
CN Diphantoin
CN Diphedan
CN Diphenylan
CN Diphenylhydantoin
CN DPH
CN Hidantal
CN Lepitoin
CN Phenytoin
CN Phenytoine
CN Sodanton
CN Zentropil
FS 3D CONCORD
DR 125-59-7
MF C15 H12 N2 O2
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, ULIDAT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



5177 REFERENCES IN FILE CA (1967 TO DATE)
95 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5184 REFERENCES IN FILE CAPLUS (1967 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:63323

REFERENCE 2: 131:58758

REFERENCE 3: 131:56155

REFERENCE 4: 131:56144

REFERENCE 5: 131:54233

REFERENCE 6: 131:53892

REFERENCE 7: 131:53545

REFERENCE 8: 131:53535

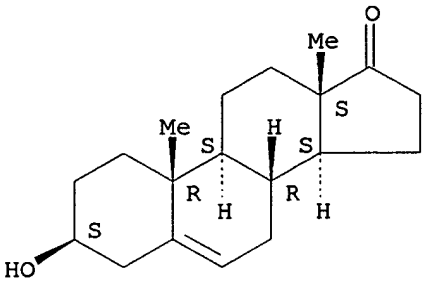
REFERENCE 9: 131:53421

REFERENCE 10: 131:39647

L146 ANSWER 8 OF 10 REGISTRY COPYRIGHT 1999 ACS
RN **53-43-0** REGISTRY
CN Androst-5-en-17-one, 3-hydroxy-, (3.beta.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Androst-5-en-17-one, 3.beta.-hydroxy- (8CI)
OTHER NAMES:
CN 17-Chetovis
CN 17-Hormoforin
CN 3.beta.-Hydroxyandrost-5-en-17-one
CN 5,6-Dehydroisoandrosterone
CN 5,6-Didehydroisoandrosterone
CN 5-Dehydroepiandrosterone
CN Androstenolone
CN Dehydro-epi-androsterone
CN Dehydroepiandrosterone
CN Dehydroisoandrosterone
CN DHA
CN DHEA
CN Diandron
CN Diandrone
CN Prasterone
CN Psicosterone
CN trans-Dehydroandrosterone
FS STEREOSEARCH
DR 9013-35-8, 105597-37-3, 108673-53-6

MF C19 H28 O2
CI COM
LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CIN, CSCHEM, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).



4696 REFERENCES IN FILE CA (1967 TO DATE)
92 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4697 REFERENCES IN FILE CAPLUS (1967 TO DATE)
93 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:63203

REFERENCE 2: 131:57229

REFERENCE 3: 131:54091

REFERENCE 4: 131:49541

REFERENCE 5: 131:44196

REFERENCE 6: 131:32088

REFERENCE 7: 131:31422

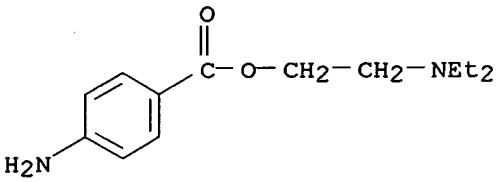
REFERENCE 8: 131:31098

REFERENCE 9: 131:28114

REFERENCE 10: 131:28110

L146 ANSWER 9 OF 10 REGISTRY COPYRIGHT 1999 ACS
RN **51-05-8** REGISTRY
CN Benzoic acid, 4-amino-, 2-(diethylamino)ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzoic acid, p-amino-, 2-(diethylamino)ethyl ester, monohydrochloride (8CI)
OTHER NAMES:

CN 2-Diethylaminoethyl p-aminobenzoate hydrochloride
CN Allocaine
CN Aminocaine
CN Anadolor
CN Anesthesol
CN Anestil
CN Atoxicocaine
CN Bernacaine
CN Cetain
CN Chlorocaine
CN Diethylaminoethanol 4-aminobenzoate hydrochloride
CN Ethocain
CN Ethocaine
CN Eugerase
CN Geriocaine
CN Gerovital H3
CN Herocaine
CN Irocaine
CN Isocain
CN Isocaine
CN Isocaine-Heisler
CN Juvocaine
CN Kerocaine
CN Lactocaine
CN Naucain
CN Naucaine
CN Neocaine
CN Neotonocaine
CN Novocain
CN Novocaine
CN Novocaine hydrochloride
CN Omnicain
CN Paracain
CN Planocaine
CN Polocaine
CN Procaine hydrochloride
CN Procaine monohydrochloride
CN Scurocaine
CN Sevicaine
CN Syncaine
CN Topokain
CN Westocaine
DR 12663-50-2, 8023-03-8, 138481-13-7, 41585-82-4
MF C13 H20 N2 O2 . Cl H
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CBNB, CIN, CSCHEM, DETHERM*, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
CRN (59-46-1)



● HCl

2243 REFERENCES IN FILE CA (1967 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2243 REFERENCES IN FILE CAPLUS (1967 TO DATE)
23 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:51393

REFERENCE 2: 131:39648

REFERENCE 3: 131:9619

REFERENCE 4: 130:301572

REFERENCE 5: 130:292512

REFERENCE 6: 130:245913

REFERENCE 7: 130:242300

REFERENCE 8: 130:242236

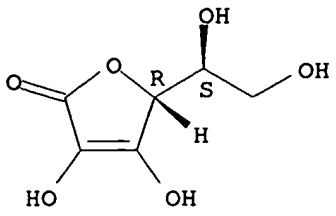
REFERENCE 9: 130:223871

REFERENCE 10: 130:223781

L146 ANSWER 10 OF 10 REGISTRY COPYRIGHT 1999 ACS
RN **50-81-7** REGISTRY
CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN (+)-Ascorbic acid
CN 3-keto-L-Gulofuranolactone
CN 3-Oxo-L-gulofuranolactone
CN Adenex
CN Allercorb
CN Antiscorbic vitamin
CN Antiscorbutic vitamin
CN Ascoltin
CN Ascorbajen
CN Ascorbic acid
CN Ascorbutina
CN Ascorin
CN Ascorteal
CN Ascorvit
CN C-Quin
CN C-Vimin

CN Cantan
CN Cantaxin
CN Catavin C
CN Ce-Mi-Lin
CN Ce-Vi-Sol
CN Cebicure
CN Cebion
CN Cebione
CN Cecon
CN Cegiolan
CN Ceglion
CN Celaskon
CN Celin
CN Cemagyl
CN Cenetone
CN Cereon
CN Cergona
CN Cescorbat
CN Cetamid
CN Cetemican
CN Cevalin
CN Cevatine
CN Cevex
CN Cevimin
CN Cevital
CN Cevitamic acid
CN Cevitamin
CN Cevitan
CN Cevitex
CN Chewcee
CN Ciamin
CN Cipca
CN Citrovit
CN Colascor
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS STEREOSEARCH
DR 56533-05-2, 57304-74-2, 57606-40-3, 56172-55-5, 129940-97-2, 14536-17-5, 50976-75-5, 89924-69-6, 30208-61-8
MF C6 H8 O6
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, APILIT, APILIT2, APIPAT, APIPAT2, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CBNB, CIN, CSCHEM, CSNB, DETHERM*, DDFU, DIPPR*, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, TULSA, ULIDAT, USAN, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



37531 REFERENCES IN FILE CA (1967 TO DATE)
898 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
37563 REFERENCES IN FILE CAPLUS (1967 TO DATE)
12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 131:67338

REFERENCE 2: 131:67290

REFERENCE 3: 131:67223

REFERENCE 4: 131:64872

REFERENCE 5: 131:64860

REFERENCE 6: 131:63564

REFERENCE 7: 131:63539

REFERENCE 8: 131:63471

REFERENCE 9: 131:63463

REFERENCE 10: 131:63317

=> fil aidsline
FILE 'AIDSLINE' ENTERED AT 14:11:25 ON 25 JUL 1999

FILE COVERS 1980 TO 14 JUL 1999 (19990714/ED)

AIDSLINE has been reloaded to reflect the annual MeSH changes made by the National Library of Medicine for 1999. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his l150-

(FILE 'AIDSLINE' ENTERED AT 14:02:05 ON 25 JUL 1999)
L150 0 S NKC482 OR NKC 482
L151 63 S PMPA OR PHOSPHONOMETHOXYPROPYL ADENINE
L152 4 S TBD
L153 13292 S L147-L152
L154 670 S L85
L155 810 S PROCAINE OR ASCORBIC ACID OR VITAMINE C OR ZINC OR LIDOCAINE
L156 2 S HYDROXYISOVALERIC OR HYDROXY BETA METHYLBUTYRIC OR HYDROXY BE
L157 20 S PHOSPHATIDYLSERINES+NT/CT
L158 573 S KETOCONAZOLE OR PREGNENOLONE OR PHENYTOIN OR CLONIDINE OR IPR

L159 121 S L153 AND L154-L158
L160 43 S L159 AND (COMBIN? OR SYNERG? OR FORMUL? OR COMPOSITION)
L161 18 S DRUG THERAPY, COMBINATION/CT AND L159
L162 25 S L160 NOT L161
L163 5 S L162 AND SYNERG?
L164 23 S L161,L163
L165 20 S L162 NOT L164

FILE 'AIDSLINE' ENTERED AT 14:11:25 ON 25 JUL 1999

=> d all tot l164

L164 ANSWER 1 OF 23 AIDSLINE
AN 1999:632 AIDSLINE
DN MED-99020568
TI The effectiveness of combined **saquinavir** and **ketoconazole** treatment in reducing HIV viral load.
AU Jordan W C
CS Department of Internal Medicine and Family Practice, Charles R. Drew University of Medicine and Science, King-Drew Medical Center, Los Angeles, California 90059, USA.
SO JOURNAL OF THE NATIONAL MEDICAL ASSOCIATION, (1998). Vol. 90, No. 10, pp. 622-4.
Journal code: J9Z. ISSN: 0027-9684.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED
LA English
OS MEDLINE 99020568
EM 199901
AB With the advent of protease inhibitors, the treatment of persons infected with the human immunodeficiency virus (HIV) has resulted in lower levels of the virus in the blood. The first of these protease inhibitors was **saquinavir**, which inhibits the HIV protease enzyme responsible for post-translational processing of Gag and Gag-Pol poly protein precursors into their functional products. Studies have suggested that **ketoconazole**, given in combination with **saquinavir**, increases the bioavailability of **saquinavir**. This study compared the HIV viral load in patients treated with **saquinavir** alone and in combination with **ketoconazole**. Results showed that while all patients who received **saquinavir** exhibited a positive response, patients who also received **ketoconazole** had a greater drop in viral load levels. In addition, a greater number of patients had undetectable viral levels after 3 months on the **ketoconazole**/**saquinavir** regimen. These results indicate that the combination of **saquinavir/ketoconazole** for the treatment of HIV requires further study.
CT Check Tags: Human
*Antifungal Agents: TU, therapeutic use
Drug Therapy, Combination
*HIV Infections: DT, drug therapy
*HIV Protease Inhibitors: TU, therapeutic use
*Ketoconazole: TU, therapeutic use
*Saquinavir: TU, therapeutic use
*Viral Load
RN 127779-20-8 (**Saquinavir**); **65277-42-1 (Ketoconazole)**
CN 0 (Antifungal Agents); 0 (HIV Protease Inhibitors)

L164 ANSWER 2 OF 23 AIDSLINE

AN 1998:14925 AIDSLINE
DN MED-98328906
TI **Nelfinavir**. A review of its therapeutic efficacy in HIV infection.
AU Jarvis B; Faulds D
CS Adis International Limited, Auckland, New Zealand. demail@adis.co.nz
SO DRUGS, (1998). Vol. 56, No. 1, pp. 147-67.
Journal code: EC2. ISSN: 0012-6667.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
FS MED; Priority Journals
LA English
OS MEDLINE 98328906
EM 199812
AB **Nelfinavir** is a selective inhibitor of HIV protease, the enzyme responsible for post-translational processing of HIV propeptides. In the presence of the drug, immature, noninfectious virus particles are produced. **Nelfinavir** in combination with nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors and/or other protease inhibitors profoundly suppresses viral replication. Plasma HIV RNA levels (viral loan) rapidly fall below the limit of detection (LOD; usually 400 or 500 copies/ml in the majority of patients. When used in combination with NRTIs, **nelfinavir** 1250mg twice daily produced similar results to 3-times-daily **nelfinavir** at a range of total daily dosages. In an ongoing study > 70% of adults receiving a **nelfinavir** based combination regimen had plasma HIV RNA levels below the LOD (< 400 copies/ml) after 84 weeks. In addition, 73% of paediatric patients receiving **nelfinavir** plus at least 1 new NRTI had viral loads below the LOD (< 400 copies/ml) after 34 weeks. Furthermore, CD4+ cell counts generally increased in conjunction with reductions in viral load. Combination therapy with **nelfinavir** and **saquinavir** results in higher **saquinavir** plasma concentrations, make twice-daily administration of **saquinavir** feasible and may delay the emergence of resistant viral strains. A unique mutation at condon 30 (D30N) of the protease gene confers resistance to **nelfinavir**, but HIV with D30N mutation remains fully susceptible to **indinavir**, **ritonavir** and **saquinavir** in vitro. Nonetheless, in clinical use, significant cross-resistance is seen with all currently available protease inhibitors. Diarrhoea is the most frequently reported adverse event in patients receiving **nelfinavir** -based combination therapy and has been reported in up to 32% of **nelfinavir** recipients in randomised trials. Diarrhoea is generally of mild to moderate severity and does not result in weight loss. Rash, nausea, headache and asthenia were each reported in < or = 5% of patients. Approximately 5% of patients enrolled in an expanded access programme in the US discontinued **nelfinavir** because of adverse events. **Nelfinavir** is metabolised by the cytochrome P450 system. Several clinically significant pharmacokinetic drug interactions between **nelfinavir** and other drugs (i.e. **ketoconazole**, rifabutin, rifabutin, rifampicin), including other protease inhibitors (i.e. **indinavir**, **ritonavir**, **saquinavir**) have been documented. As with other available protease inhibitors, hyperglycaemia, hyperlipidaemia and abnormal fat distribution have been reported, albeit infrequently, in association with **nelfinavir**. Conclusion: **Nelfinavir**-based combination regimens are well tolerated and produce profound and prolonged suppression of HIV replication in adult and paediatric patients. Hence, **nelfinavir**

is suitable for inclusion in antiretroviral regimens for initial therapy for HIV infection and, alternatively, in regimens for patients unable to tolerate other protease inhibitors.

CT Check Tags: Human
Adult
Anti-HIV Agents: AD, administration & dosage
Anti-HIV Agents: PD, pharmacology
*Anti-HIV Agents: TU, therapeutic use
Child
Child, Preschool
Drug Interactions
Drug Resistance, Microbial
Drug Therapy, Combination
Drug Tolerance
HIV: DE, drug effects
*HIV Infections: DT, drug therapy
Nelfinavir: AD, administration & dosage
Nelfinavir: PD, pharmacology
***Nelfinavir**: TU, therapeutic use

RN 159989-64-7 (**Nelfinavir**)
CN 0 (Anti-HIV Agents)

L164 ANSWER 3 OF 23 AIDSLINE
AN 1998:12245 AIDSLINE
DN AIDS-98703570
TI Novel approaches for the treatment of HIV.
AU Arroyo H T
SO PWA Newsline, (1998). pp. 16-7.
ISSN: 1069-3637.
CY United States
DT (NEWSLETTER ARTICLE)
FS AIDS
LA English
EM 199809
AB Presentations at the Fifth Conference on Retroviruses and Opportunistic Infections focused on new and novel HIV treatments. Four new agents in advanced testing are described: **abacavir** (1592), **efavirenz** (DMP-266), **adefovir** dipivoxil (bis-POM PMEA), and amprenavir (141W94). Other new drugs are being developed; however, the drugs are not as far along in the testing and approval process. The new drugs include integrase inhibitors, **zinc** finger inhibitors, cyclams and bycyclams, fusion inhibitors, and CKR-5 gene therapy. A summary of each drug is provided.

CT Adenine: AE, adverse effects
Adenine: TU, therapeutic use
Anti-HIV Agents: AE, adverse effects
*Anti-HIV Agents: TU, therapeutic use
Dideoxynucleosides: AE, adverse effects
Dideoxynucleosides: TU, therapeutic use
Drug Resistance, Microbial
Drug Therapy, Combination
Gene Therapy
Heterocyclic Compounds: TU, therapeutic use
*HIV Infections: DT, drug therapy
HIV Integrase Inhibitors: TU, therapeutic use
HIV Protease Inhibitors: AE, adverse effects
*HIV Protease Inhibitors: TU, therapeutic use
Oxazines: AE, adverse effects
Oxazines: TU, therapeutic use

Receptors, Chemokine: AI, antagonists & inhibitors
Reverse Transcriptase Inhibitors: AE, adverse effects
*Reverse Transcriptase Inhibitors: TU, therapeutic use
Sulfonamides: AE, adverse effects
Sulfonamides: TU, therapeutic use
Zinc Fingers
RN 154635-17-3 (L 743726); 161814-49-9 (VX 478); 73-24-5 (Adenine)
CN 0 (Anti-HIV Agents); 0 (Heterocyclic Compounds); 0 (HIV Integrase Inhibitors); 0 (HIV Protease Inhibitors); 0 (Receptors, Chemokine); 0 (Reverse Transcriptase Inhibitors); 0 (1592U89)

L164 ANSWER 4 OF 23 AIDSLINE
AN 1998:8972 AIDSLINE
DN MED-98195465
TI **Saquinavir**. Clinical pharmacology and efficacy.
AU Vella S; Floridia M
CS Laboratory of Virology, Istituto Superiore di Sanit`a, Rome, Italy.
SO CLINICAL PHARMACOKINETICS, (1998). Vol. 34, No. 3, pp. 189-201.
Journal code: DG5. ISSN: 0312-5963.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
FS MED; Priority Journals
LA English
OS MEDLINE 98195465
EM 199807
AB **Saquinavir** is an HIV protease inhibitor with no, or limited, effect on the activity of other structurally related human aspartic proteinases. As with other HIV protease inhibitors, **saquinavir** inhibits the cleavage of the gag-pol protein substrate leading to the release of structurally defective and functionally inactive viral particles. It is active on both HIV-1 and HIV-2, and also has activity on chronically infected cells and HIV strains resistant to reverse transcriptase inhibitors. **Synergy** of action has been observed with other antiretroviral drugs. **Saquinavir** is characterised by a low bioavailability which is further reduced in the fasting state. Metabolism is mainly hepatic through cytochrome P450 (CYP) 3A4, but intestinal metabolism through the same system has also been reported. To achieve higher drug plasma concentrations and increase the antiviral effect, a new **formulation** of **saquinavir** with a higher bioavailability has recently been introduced. Higher plasma drug concentrations may also be obtained by **combining** the drug with CYP blockers, such as **ritonavir** or **ketoconazole**. Because of its metabolic interference with the CYP system, **saquinavir** cannot be coadministered with astemizole, terfenadine or cisapride. Rifampicin (rifampin) is also contraindicated because coadministration can lead to decreases in **saquinavir** concentrations. Interactions have also been reported with other drugs metabolised through the same system, including non-nucleoside reverse transcriptase inhibitors and HIV protease inhibitors. Resistance has been observed after both in vitro and in vivo drug exposure, with a relatively specific mutation profile compared with other protease inhibitors. **Saquinavir** is generally well tolerated, with mild gastrointestinal symptoms representing the most commonly observed adverse effects. Although characterized by low bioavailability, in phase III trials **saquinavir** has been shown to have clinical efficacy in terms of survival and progression rate. As with the other protease inhibitors, **saquinavir** should be used in **combination** with other

antiretroviral drugs. Current therapeutic guidelines, however, recommend the selection of an initial treatment regimen with other protease inhibitors with higher in vivo activity in terms of RNA and CD4 response. The results of ongoing studies will clarify to what extent a new **saquinavir formulation**, recently introduced, is superior to the previous one in terms of antiviral activity and to provide comparisons with other protease inhibitors. Further studies are also needed to define the best place of **saquinavir** within treatment strategies based on protease inhibitors, particularly in respect to the optimal sequence for its use with other protease inhibitors, and the dynamics of cross-resistance and its role within regimens based on the **combination** of protease inhibitors.

CT Check Tags: Human
Anti-HIV Agents: PK, pharmacokinetics
*Anti-HIV Agents: TU, therapeutic use
*HIV Infections: DT, drug therapy
HIV Protease Inhibitors: PK, pharmacokinetics
*HIV Protease Inhibitors: TU, therapeutic use
Saquinavir: PK, pharmacokinetics
***Saquinavir**: TU, therapeutic use
Virus Replication: DE, drug effects

RN 127779-20-8 (**Saquinavir**)

CN 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors)

L164 ANSWER 5 OF 23 AIDSLINE

AN 1998:7899 AIDSLINE

DN AIDS-98929345

TI Evidence of unique metabolic effects of protease inhibitors.

AU Mulligan K; Tai V W; Algren H; Chernoff D N; Lo J C; Schambelan M

CS University of California, San Francisco, CA.

SO 5th Conf Retrovir Oppor Infect, (1998). pp. 157 (Abstract No. 414).

CY United States

DT (MEETING ABSTRACTS)

FS AIDS

LA English

EM 199806

AB Anecdotal reports of changes in lipid and carbohydrate (CHO) metabolism in patients on protease inhibitors (PI) have prompted speculation that these drugs have unique metabolic effects. To determine whether there are metabolic effects that are associated only with this class of antiretrovirals (ARV), we compared results obtained in patients before and after beginning an ARV regimen that included a PI (N=16 [13M, 3F]) or **lamivudine** (**3TC**; N=8 [7M, 1F) and in a matched control group on stable ARV other than **3TC** or PI or no ARV (CNTRL; N=16 [13M, 3F]). The PI group included 12 patients on **indinavir**, 2 on **saquinavir**, and 2 on **ritonavir**, in combination with reverse transcriptase inhibitors. The mean duration of therapy at followup was 4.4 plus or minus 0.8 and 3.9 plus or minus 1.0 months in PI and **3TC**, respectively. CD4+ lymphocyte count increased in PI and **3TC** (+68 plus or minus 33 and +102 plus or minus 33 cells/microliter; p=0.030 and 0.009, respectively). Viral load became undetectable in 69% of patients on PI and 25% on **3TC** (p=0.08). Glucose, triglyceride, and cholesterol levels increased significantly in PI (+14 plus or minus 4, +75 plus or minus 35, +51 plus or minus 10 mg/dl; p=0.03, 0.002, and less than 0.001, respectively) but not in **3TC** or CNTRL. Similarly, insulin levels increased in PI (+18.6 plus or minus 9.5 microniU/ml; p=0.07) but not in **3TC** or CNTRL. Testosterone, cortisol, and **DHEA** sulfate levels did not change significantly in any group. Weight tended to increase in each group (+1.2 plus or minus

1.2, +0.5 plus or minus 0.8, and +0.6 plus or minus 0.9 kg in PI, **3TC**, and CNTRL, respectively). There were no significant changes in total or regional fat or lean body mass (dual-energy X-ray absorptiometry) in any group over this short time period. These results suggest that protease inhibitors have unique metabolic effects that are independent of improvements in CD4 count or nutritional status. However, it is possible that more effective viral suppression with PI therapy may play a role in these changes in lipid and CHO metabolism.

CT Check Tags: Comparative Study; Female; Human; Male
*Adipose Tissue: PA, pathology
Blood Glucose: AN, analysis
Cholesterol: BL, blood
Densitometry, X-Ray
Drug Therapy, Combination
HIV Infections: DT, drug therapy
*HIV Infections: ME, metabolism
*HIV Protease Inhibitors: AE, adverse effects
HIV Protease Inhibitors: TU, therapeutic use
Lipids: ME, metabolism

RN 57-88-5 (Cholesterol)

CN 0 (Blood Glucose); 0 (HIV Protease Inhibitors); 0 (Lipids)

L164 ANSWER 6 OF 23 AIDSLINE

AN 1998:7837 AIDSLINE

DN AIDS-98929283

TI Predictions of anti-AIDS drug-interactions using human liver microsomes.

AU Wang Y; Hickman D; Takahashi C; Ambrocio D; Unadkat J D

CS University of Washington, Seattle, WA.

SO 5th Conf Retrovir Oppor Infect, (1998). pp. 146 (Abstract No. 357).

CY United States

DT (MEETING ABSTRACTS)

FS AIDS

LA English

EM 199806

AB Aim: Multiple drug therapies for AIDS and its associated opportunistic infections have exponentially increased the numbers of possible drug interactions. Thus, as a part of an ongoing series of studies, we have examined the utility of using human liver microsomes to predict clinically relevant metabolic drug interactions. Methods: We have determined cytochrome P450 (CYP) inhibitory capacities of azithromycin (AZ), atovaquone (ATQ), clarithromycin (CLA), dapsone (DDS), ethambutol (EB), fluconazole (FLU), **ketoconazole** (KET), isoniazid (INH), **indinavir** (IND), rifabutin (RFB), rifampin (RFP), **saquinavir** (SAQ), sulfamethoxazole (SMX), sulfadiazine (SDZ) and **zidovudine** (**AZT**), towards CYP1A2, 2A6, 2C9, 2C19, 2D6, 2E1 and 3A4/5 activities. Results: Of the drugs examined to date, at clinical concentration only SMX (400 micrograms/ml) and SDZ (400 micrograms/ml) significantly (greater than 30%) inhibited CYP2A6 (by 36 and 78% respectively); ATQ (50 micrograms/ml) and FLU (8 micrograms/ml) inhibited CYP2C9 by 62 and 49%. IND and KET inhibited CYP3A4/5 by 41 and 50%, respectively. In addition, at ten-fold the clinical concentration, RFP (300 micrograms/ml) inhibited both 2A6 and 2D6 by 30%. INH (75 micrograms/ml) and KET (75 micrograms/ml) inhibited 2E1 and 2C9 by 52 and 63%. FLU (80 micrograms/ml) inhibited 3A4/5 activity by 55%. Based on these data, we predict that both SMX and SDZ will lead to clinically significant drug interactions when co-administrated with drugs primarily cleared by 2A6 metabolism. Likewise, ATQ and FLU will interact with drugs cleared by 2C9. IND and KET will interact with drugs which are cleared by 3A4/5. In the clinic KET and IND are potent inhibitors of metabolic

clearances of SAQ and CLA (both CYP3A4 substrates), respectively. Collectively, our data indicate that human liver microsomes are predictive of clinically significant drug interactions observed in the clinic.

CT Check Tags: Human
Acquired Immunodeficiency Syndrome: DT, drug therapy
*Anti-HIV Agents: PK, pharmacokinetics
AIDS-Related Opportunistic Infections: DT, drug therapy
Cytochrome P-450: AI, antagonists & inhibitors
*Cytochrome P-450: ME, metabolism
*Drug Interactions
Drug Therapy, Combination
*Microsomes, Liver: ME, metabolism
Predictive Value of Tests

RN 9035-51-2 (Cytochrome P-450)
CN 0 (Anti-HIV Agents)

L164 ANSWER 7 OF 23 AIDSLINE
AN 1997:21676 AIDSLINE
DN MED-97354392
TI Rifabutin absorption in the gut unaltered by concomitant administration of **didanosine** in AIDS patients.
AU Li R C; Narang P K; Sahai J; Cameron W; Bianchine J R
CS Department of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Shatin. ronli@cuhk.edu.hk
SO ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1997). Vol. 41, No. 7, pp. 1566-70.
Journal code: 6HK. ISSN: 0066-4804.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 97354392
EM 199711
AB **Didanosine** (**ddI**) is currently used in the management of patients infected by the human immunodeficiency virus. Rifabutin (RBT) is being extensively used for prophylaxis against Mycobacterium avium complex (MAC) infections. Due to its acid-labile characteristics, **ddI** must be administered with a buffer. Recent reports have indicated that absorption of **ketoconazole**, ciprofloxacin, and dapsone, etc., in the gut is altered by concomitant **ddI** dosing. We have assessed whether concomitant dosing of **ddI** as antiretroviral therapy modifies RBT absorption in the gut, its steady-state pharmacokinetics, and/or safety in 15 patients with AIDS. Of the 15 patients enrolled, 12 completed the study and 3 receiving 600 mg of RBT with concomitant **ddI** administration withdrew prematurely from the study. Steady-state RBT pharmacokinetics were assessed on day 13 (**ddI** plus RBT) and day 16 (RBT alone). The **ddI** doses (adjusted for body weight) were 167 to 375 mg twice daily, while RBT was administered as a single 300- or 600-mg daily dose. No statistically significant ($P > 0.05$) differences were seen in RBT absorption parameter estimates between days 13 and 16: maximum concentration in plasma (Cmax; 511 +/- 341 ng/ml versus 525 +/- 254 ng/ml) and the time at which Cmax was observed (3.0 versus 2.5 h). The mean RBT estimates for area under the concentration-time curve from 0 to 24 h (AUC(0-tau)) (5,650 versus 5,023 ng x h/ml) and for oral clearance (1.28 versus 1.18 liter/h/kg) on both study days were also similar. Assessment based on urinary recovery of RBT (3.1 versus 3.7 mg) and its predominant deacetyl metabolite, LM565 (1.6 versus 1.4 mg), showed no apparent effect of **ddI**. The fraction

of the RBT dose converted to LM565, as suggested by the ratio of AUC of the metabolite to AUC of the parent drug, was also unaltered (0.15 versus 0.12). A ratio analysis (day 13/day 16) of the RBT pharmacokinetic estimates showed that the 95% confidence intervals for all parameters were inclusive of one. Furthermore, the brief interruption of **ddI** therapy over this short study period at steady state produced no clinically significant changes in body weight, hematology, and renal and pancreatic functions. Therefore, concomitant administration of **ddI** appears not to affect RBT absorption in the gut and its disposition or safety in patients with AIDS.

CT Check Tags: Female; Human; Male
*Acquired Immunodeficiency Syndrome: DT, drug therapy
Acquired Immunodeficiency Syndrome: ME, metabolism
Adult
*Anti-HIV Agents: TU, therapeutic use
*Antibiotics, Antitubercular: PK, pharmacokinetics
*Didanosine: TU, therapeutic use
Drug Interactions
Drug Therapy, Combination
*Intestinal Absorption: PH, physiology
Middle Age
Mycobacterium avium-intracellulare Infection: PC, prevention & control
Rifabutin: AE, adverse effects
*Rifabutin: PK, pharmacokinetics
RN 69655-05-6 (**Didanosine**); 72559-06-9 (Rifabutin)
CN 0 (Anti-HIV Agents); 0 (Antibiotics, Antitubercular)

L164 ANSWER 8 OF 23 AIDSLINE
AN 1997:15076 AIDSLINE
DN MED-97173271
TI SRR-SB3, a disulfide-containing macrolide that inhibits a late stage of the replicative cycle of human immunodeficiency virus.
AU Witvrouw M; Balzarini J; Pannecouque C; Jhaumeer-Laulloo S; Este J A; Schols D; Cherepanov P; Schmit J C; Debyser Z; Vandamme A M; Desmyter J; Ramadas S R; de Clercq E
CS Rega Institute for Medical Research, Katholieke Universiteit Leuven, Belgium.
SO ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, (1997). Vol. 41, No. 2, pp. 262-8. Journal code: 6HK. ISSN: 0066-4804.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 97173271
EM 199707
AB From a series of macrocyclic diamides possessing the disulfide linkage, only SRR-SB3, a compound that complexes with **zinc**, was found to inhibit human immunodeficiency virus type 1 (HIV-1; strain IIIB) replication at a concentration of 1.8 to 6.5 micrograms/ml in MT-4, CEM, and peripheral blood mononuclear cells. SRR-SB3 was toxic to MT-4 cells at a concentration of 15.9 micrograms/ml, resulting in a selectivity index of 9 in these cells. This macrolide was also effective against various other HIV-1 strains, including clinical isolates and HIV-1 strains resistant to protease inhibitors and nucleoside and nonnucleoside reverse transcriptase inhibitors. It was also active against various HIV-2 strains, simian immunodeficiency virus (strain MAC251), and Moloney murine sarcoma virus, but not against viruses other than retroviruses. In addition, the compound was found to inhibit chronic HIV-1 infections in vitro. The compound in **combination** with other antiviral agents, such as

zidovudine, **zalcitabine**, and **stavudine**, showed an effect that was between additive and **synergistic**. Time-of-addition experiments indicated that SRR-SB3 acts at a late stage of the HIV-1 replicative cycle.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
*Anti-HIV Agents: PD, pharmacology
*Benzamides: PD, pharmacology
Cell Line
*Disulfides: PD, pharmacology
Drug **Synergism**
DNA, Viral: AN, analysis
*HIV-1: DE, drug effects
HIV-1: PH, physiology
Mice
Moloney Sarcoma Virus: DE, drug effects
Polymerase Chain Reaction
Retroviridae Infections: DT, drug therapy
Retroviridae Infections: VI, virology
Reverse Transcriptase Inhibitors: PD, pharmacology
Sarcoma, Experimental: DT, drug therapy
Sarcoma, Experimental: VI, virology
Tumor Virus Infections: DT, drug therapy
Tumor Virus Infections: VI, virology
*Virus Replication: DE, drug effects

CN 0 (Anti-HIV Agents); 0 (Benzamides); 0 (Disulfides); 0 (DNA, Viral); 0 (Reverse Transcriptase Inhibitors); 0 (SRR SB3)

L164 ANSWER 9 OF 23 AIDSLINE
AN 1997:654 AIDSLINE
DN ICA11-96921420
TI The Canadian randomized open-label trial of combination therapy for MAC bacteremia: characteristics and outcome of subjects with negative blood cultures at baseline.
AU Zarowny D; Thorne A; Khorasheh S; Shafran S; Toma E; Miller M; Duperval R; Smaill F; Lemieux C; Cameron W; Schlech W; Mackie I; McFadden D; Kamal M; DiPietro N
CS Canadian HIV Trials Network, Vancouver, Canada. Fax: 604- 631 5210. E-mail:. don@hivnet.ubc.ca.
SO Int Conf AIDS, (1996). Vol. 11, No. 1, pp. 117 (Abstract No. Mo.B.1357).
CY Canada
DT (MEETING ABSTRACTS)
FS ICA11
LA English
EM 199701
AB Objective: A randomized open-label trial showed that a three drug arm of clarithromycin 1000 mg BID, rifabutin 600/300 mg QD, and ethambutol 15 mg/kg QD was associated with significantly more frequent and faster clearance of bacteremia and increased survival compared to a four drug arm (ciprofloxacin, ethambutol, rifampin, and clofazimine) in HIV+ patients with Mycobacterium avium complex. This subanalysis describes the characteristics and outcome of patients recruited to the trial who had negative baseline blood cultures for MAC and were not included in the primary analysis, and compares them to the cohort who were baseline positive. Methods: Eligible patients with positive blood cultures done at their local clinical facility were enrolled. Enrollment cultures were then obtained and shipped to a central laboratory for quantitative culture using BACTEC and conventional methods and speciation by DNA probe. Patients were treated and followed intensively for 16 weeks with additional blood cultures. Investigational drug treatment was available

for life. Post-study follow-up was done to obtain survival information. Descriptive statistics were used to characterize the two groups (central lab negative versus central lab positive) at randomization. Survival was compared by using the log rank test. Results: Of 229 patients randomized, 8 were ineligible or had non-MAC mycobacteremia, 34 (15%) had negative blood cultures in the specimens sent to the central lab and 187 (82%) were baseline positive. The negative and positive groups were similar in age (36.9 yrs. versus 38.2), gender (94% male), previous rifabutin prophylaxis (32% versus 23%), median CD4 count (10 cells /mm3) and median Karnofsky (70). The baseline culture negative group was heavier (mean weight 63.8 kg versus 58.8, p is less than .05), were less frequent users of **ketoconazole** (p less than .05) and showed trends to greater use of **ddC** and **AZT** (p=.05 and p=.07 respectively). In 32 of the 34 subjects at least one post-baseline culture was obtained. One or more of these cultures were positive for MAC in 6 of the 32. While the difference in survival was not significant (p=.27), a somewhat longer median survival was observed in the negatives (9.1 vs 6.6 months). Conclusion: There was no difference in survival between HIV+ patients with baseline negative or intermittently positive blood cultures and patients with positive baseline cultures in a prospective randomized trial of two treatment regimens for M. avium complex infection.

CT Check Tags: Female; Human; Male
Adult
Anti-Infective Agents: AD, administration & dosage
*Anti-Infective Agents: TU, therapeutic use
Antiviral Agents: AD, administration & dosage
Antiviral Agents: TU, therapeutic use
Canada
Ciprofloxacin: AD, administration & dosage
Ciprofloxacin: TU, therapeutic use
Clofazimine: AD, administration & dosage
Clofazimine: TU, therapeutic use
Drug Therapy, Combination
Ethambutol: AD, administration & dosage
Ethambutol: TU, therapeutic use
HIV Infections: CO, complications
HIV Infections: DT, drug therapy
Karnofsky Performance Status
*Mycobacterium avium Complex: IP, isolation & purification
*Mycobacterium avium-intracellulare Infection: DT, drug therapy
Rifampin: AD, administration & dosage
Rifampin: TU, therapeutic use
Treatment Outcome
Zalcitabine: AD, administration & dosage
Zalcitabine: TU, therapeutic use
Zidovudine: AD, administration & dosage
Zidovudine: TU, therapeutic use

RN 13292-46-1 (Rifampin); 2030-63-9 (Clofazimine); 30516-87-1 (**Zidovudine**); 74-55-5 (Ethambutol); 7481-89-2 (**Zalcitabine**); 85721-33-1 (Ciprofloxacin)

CN 0 (Anti-Infective Agents); 0 (Antiviral Agents)

L164 ANSWER 10 OF 23 AIDSLINE
AN 1996:11946 AIDSLINE
DN MED-96330673
TI Drug interactions with antiviral drugs.
AU Taburet A M; Singlas E
CS Hopital Bicetre, Le Kremlin-Bicetre, France.
SO CLINICAL PHARMACOKINETICS, (1996). Vol. 30, No. 5, pp. 385-401.

Journal code: DG5. ISSN: 0312-5963.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
FS MED; Priority Journals
LA English
OS MEDLINE 96330673
EM 199612
AB Antiviral drug interactions are a particular problem among immuno-compromised patients because these patients are often receiving multiple different drugs, i.e. antiretroviral drugs and drugs effective against herpesvirus. The combination of **zidovudine** and other antiretroviral drugs with different adverse event profiles, such as **didanosine**, **zalcitabine** and **lamivudine**, appears to be well tolerated and no relevant pharmacokinetic interactions have been detected. The adverse effects of **didanosine** and **zalcitabine** (i.e. peripheral neuropathy and pancreatitis) should be taken into account when administering these drugs with other drugs with the same tolerability profile. Coadministration of **zidovudine** and ganciclovir should be avoided because of the high rate of haematological intolerance. In contrast, **zidovudine** and foscarnet have synergistic effect and no pharmacokinetic interaction has been detected. No major change in **zidovudine** pharmacokinetics was seen when the drug was combined with aciclovir, famciclovir or interferons. However, concomitant use of **zidovudine** and ribavirin is not advised. Although no pharmacokinetic interaction was documented when **didanosine** was first administered with intravenous ganciclovir, recent studies have shown that concentration of **didanosine** are increased by 50% or more when coadministered with intravenous or oral ganciclovir. The mechanism of this interaction has not been elucidated. Lack of pharmacokinetic interaction was demonstrated between foscarnet and **didanosine** or ganciclovir. Clinical trials have shown that **zidovudine** can be administered safely with paracetamol (acetaminophen), nonsteroidal anti-inflammatory drugs, oxazepam or codeine. Inhibition of **zidovudine** glucuronidation has been demonstrated with fluconazole, atovaquone, valproic acid (valproate sodium), methadone, probenecid and inosine pranobex; however, the clinical consequences of this have not been fully investigated. No interaction has been demonstrated with **didanosine** per se but care should be taken of interaction with the high pH buffer included in the tablet formulation. Drugs that need an acidic pH for absorption (**ketoconazole**, itraconazole but not fluconazole, dapsone, pyrimethamine) or those that can be chelated by the ions of the buffer (quinolones and tetracyclines) should be administered 2 hours before or 6 hours after **didanosine**. Very few interaction studies have been undertaken with other antiviral drugs. Coadministration of **zalcitabine** with the antacid 'Maalox' results in a reduction of its absorption. Dapsone does not influence the disposition of **zalcitabine**. Cotrimoxazole (trimethoprim-sulfamethoxazole) causes an increase in **lamivudine** concentrations by 43%. **Saquinavir**, delavirdine and atevirdine appeared to be metabolised by cytochrome P450 and interactions with enzyme inducers or inhibitors could be anticipated. Some studies showed that interferons can reduce drug metabolism but only a few studies have evaluated the pathways involved. Further studies are required to better understand the clinical consequences of drug interactions with antiviral drugs. Drug-drug interactions should be considered in addition to individual drug clinical benefits and safety profiles.

Analysis of Variance
*Antiviral Agents: TU, therapeutic use
*AIDS-Related Opportunistic Infections: DT, drug therapy
AIDS-Related Opportunistic Infections: IM, immunology
AIDS-Related Opportunistic Infections: MI, microbiology
CD4 Lymphocyte Count
Drug Therapy, Combination
Severity of Illness Index
Thymic Factor, Circulating: ME, metabolism
Time Factors
Treatment Outcome
***Zidovudine**: TU, therapeutic use
Zinc: AD, administration & dosage
Zinc: BL, blood
***Zinc**: TU, therapeutic use
RN 30516-87-1 (**Zidovudine**); **7440-66-6 (Zinc)**; 78922-62-0 (Thymic Factor, Circulating)
CN 0 (Antiviral Agents)

L164 ANSWER 12 OF 23 AIDSLINE
AN 1996:1992 AIDSLINE
DN MED-96008522
TI Drugs for AIDS and associated infections.
AU Anonymous
SO MEDICAL LETTER ON DRUGS AND THERAPEUTICS, (1995). Vol. 37, No. 959, pp. 87-94.
Journal code: M52. ISSN: 0025-732X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Abridged Index Medicus Journals; Priority Journals
LA English
OS MEDLINE 96008522
EM 199601
CT Check Tags: Human
*Acquired Immunodeficiency Syndrome: DT, drug therapy
Amphotericin B: TU, therapeutic use
Antibiotics, Antifungal: TU, therapeutic use
Antifungal Agents: TU, therapeutic use
Antiprotozoal Agents: TU, therapeutic use
*Antiviral Agents: TU, therapeutic use
*AIDS-Related Opportunistic Infections: DT, drug therapy
*Candidiasis, Oral: DT, drug therapy
Clindamycin: TU, therapeutic use
Clotrimazole: TU, therapeutic use
*Cryptosporidiosis: DT, drug therapy
*Cytomegalovirus Infections: DT, drug therapy
Dapsone: TU, therapeutic use
Didanosine: TU, therapeutic use
Drug Combinations
Drug Therapy, Combination
Fluconazole: TU, therapeutic use
Flucytosine: TU, therapeutic use
Folic Acid Antagonists: TU, therapeutic use
Foscarnet: TU, therapeutic use
Glucuronates: TU, therapeutic use
*Herpes Simplex: DT, drug therapy
Herpes Zoster: DT, drug therapy
Isoniazid: TU, therapeutic use
Itraconazole: TU, therapeutic use

Ketoconazole: TU, therapeutic use
*Mycobacterium avium-intracellulare Infection: DT, drug therapy
Naphthoquinones: TU, therapeutic use
Nystatin: TU, therapeutic use
Pentamidine: TU, therapeutic use
*Pneumocystis carinii Infections: DT, drug therapy
Pneumonia, Pneumocystis carinii: DT, drug therapy
Prednisone: TU, therapeutic use
Primaquine: TU, therapeutic use
Reverse Transcriptase Inhibitors: TU, therapeutic use
Stavudine: TU, therapeutic use
*Syphilis: DT, drug therapy
*Toxoplasmosis: DT, drug therapy
Toxoplasmosis: PC, prevention & control
Trimetrexate: AA, analogs & derivatives
Trimetrexate: TU, therapeutic use
*Tuberculosis: DT, drug therapy
Tuberculosis: PC, prevention & control
Zalcitabine: AA, analogs & derivatives
Zalcitabine: TU, therapeutic use
Zidovudine: AE, adverse effects
Zidovudine: TU, therapeutic use

RN 100-33-4 (Pentamidine); 134678-17-4 (**Lamivudine**); 1397-89-3 (Amphotericin B); 1400-61-9 (Nystatin); 18323-44-9 (Clindamycin); 2022-85-7 (Flucytosine); 23593-75-1 (Clotrimazole); 30516-87-1 (**Zidovudine**); 3056-17-5 (**Stavudine**); 4428-95-9 (Foscarnet); 52128-35-5 (Trimetrexate); 53-03-2 (Prednisone); 54-85-3 (Isoniazid); **65277-42-1 (Ketoconazole)**; 69655-05-6 (**Didanosine**); 7481-89-2 (**Zalcitabine**); 80-08-0 (Dapsone); 82952-64-5 (trimetrexate glucuronate); 84625-61-6 (Itraconazole); 86386-73-4 (Fluconazole); 90-34-6 (Primaquine); 94015-53-9 (atovaquone)

CN 0 (Antibiotics, Antifungal); 0 (Antifungal Agents); 0 (Antiprotozoal Agents); 0 (Antiviral Agents); 0 (Drug Combinations); 0 (Folic Acid Antagonists); 0 (Glucuronates); 0 (Naphthoquinones); 0 (Reverse Transcriptase Inhibitors)

L164 ANSWER 13 OF 23 AIDSLINE
AN 1995:13250 AIDSLINE
DN AIDS-95920108
TI A new class of anti-viral drugs attack highly conserved **zinc** fingers in retroviral nucleocapsid proteins.
AU Henderson L E; Sowder RC I I; Kane B; Casas-Finet J R; Arthur L O; Rice W G
CS PRI/DynCorp, NCI-FCRDC, Frederick MD.
SO Natl Conf Hum Retroviruses Relat Infect (2nd), (1995). pp. 68.
CY United States
DT (MEETING ABSTRACTS)
FS AIDS
LA English
EM 199512
AB All nucleocapsid (NC) proteins of the Oncovirinae and Lentivirinae subfamilies of Retroviridae contain sequences of 14 amino acids with 4 invariant residues, Cys(X)(2)Cys(X)(4)His(X)(4)Cys, which chelate **zinc** through histidine imidazole and cysteine thiolates. These structures are referred to as retroviral CCHC **zinc** fingers and are one of the most highly conserved features of the Retroviridae family. HIV-1 NC contains two **zinc** fingers separated by only 7 amino acids, and mutational analysis has shown that both are required for packaging genomic RNA and are also essential in the infection process.

Retroviral CCHC **zinc** fingers are ideal targets for rational drug design because of their extreme conservation among Retroviridae and their essential roles in two steps of viral replication. A study of reactions of cysteine thiols in HIV-INC **zinc** fingers reveals their susceptibility to attack by variety of electrophilic reagents including nitric oxide (NO), Cu(+2), Fe(+3), N-ethyl maleimide, 3-nitrosobenzamide, 5,5'- dithiobis(2-nitrobenxoic acid), iodoacetamide and many proprietary reagents identified through the NCI Drug Discovery Program. These reactions displace **zinc**, convert the thiolates to disulfides or alkylated derivatives and destroy the active conformation of the **zinc** fingers. Some but not all reagents are capable of reacting with the NC protein in the virus. Among the proprietary reagents are compounds that are non-toxic to cells in vitro, effective against laboratory and field isolates of HIV-1 (including monocytotropic strains and strains resistant to other drugs such as **AZT**, Pyridinone, **Nevirapine**), HIV-2 and SIV. Active compounds block assembly of new virus from infected cells, inactivate cell free virus, modify NC in the virus and show **synergy** in **combination** with **AZT** . Since these drugs attack highly conserved structures they may circumvent emergence of drug resistant strains.

CT Amino Acid Sequence
*Antiviral Agents: PD, pharmacology
*Capsid: CH, chemistry
Conserved Sequence
*HIV-1: CH, chemistry
*HIV-2: CH, chemistry
Molecular Sequence Data
*SIV: CH, chemistry
***Zinc** Fingers

CN 0 (Antiviral Agents); 0 (Capsid)

L164 ANSWER 14 OF 23 AIDSLINE
AN 1994:11616 AIDSLINE
DN ICA10-94369780
TI **DHEA**: a potential treatment for HIV disease.
AU Hasheeve D; Salvato P; Thompson C
CS Houston Immuno. Institute, TX.
SO Int Conf AIDS, (1994). Vol. 10, No. 1, pp. 223 (Abstract No. PB0322).
CY Japan
DT (MEETING ABSTRACTS)
FS ICA10
LA English
EM 199412
AB OBJECTIVE: To evaluate the use of **Dehydroepiandrosterone** (**DHEA**), a testosterone precursor with possible immunomodulating affects, as an adjunct therapy for HIV disease. METHODS: 12 pts. with AIDS were treated with **DHEA** in addition to standard antiviral and prophylactic OI therapy for HIV infection. (2:CD4 < 50; 6:CD4 50-100; 4:CD4 101-200). In addition to **DHEA**, 4 pts. were receiving **AZT/DDC**, 2 were on **AZT** alone, 3 were on **DDI** alone, 1 was on **AZT/DDI**, and 2 were not receiving antivirals. Pts. received an average oral **DHEA** dosage of 75 mg qd. CD4/CD8 counts were obtained at baseline and at one month intervals. Pts. were followed from 4 to 12 months with a mean of 8 months. RESULTS: 2 pts. were deceased at the end of 12 months. 9 of the remaining 10 pts. demonstrated an increase in CD4 count. 5 of the 9 (56%) demonstrated a > 25% increase in CD4 count. 8 pts. (68%) experienced an increase in CD8 count; 2 (17%) demonstrated a > 25% increase in CD8 count. CONCLUSIONS: The majority of pts. on **DHEA** adjunct therapy

experienced an increase in both CD4 and CD8 counts. A > 25% increase in CD4 count is clinically significant. How this increase relates to survival is unknown. Some reports equate increase in CD8 counts with long term survival. A randomized clinical trial of this drug appears warranted.

CT Check Tags: Human
Acquired Immunodeficiency Syndrome: DT, drug therapy
*Acquired Immunodeficiency Syndrome: TH, therapy
*Adjuvants, Immunologic: TU, therapeutic use
Anti-Infective Agents: TU, therapeutic use
Antiviral Agents: TU, therapeutic use
Combined Modality Therapy
CD4-Positive T-Lymphocytes
Didanosine: AD, administration & dosage
Didanosine: TU, therapeutic use
Drug Evaluation
Drug Therapy, Combination
Leukocyte Count: DE, drug effects
***Prasterone**: TU, therapeutic use
Treatment Outcome
Zidovudine: AD, administration & dosage
Zidovudine: TU, therapeutic use

RN 30516-87-1 (**Zidovudine**); **53-43-0 (Prasterone)**; 69655-05-6 (**Didanosine**)

CN 0 (Adjuvants, Immunologic); 0 (Anti-Infective Agents); 0 (Antiviral Agents)

L164 ANSWER 15 OF 23 AIDSLINE

AN 1994:1298 AIDSLINE

DN MED-94043874

TI Pharmacokinetics of **didanosine** and **ketoconazole** after coadministration to patients seropositive for the human immunodeficiency virus.

AU Knupp C A; Brater D C; Relue J; Barbhaiya R H

CS Department of Metabolism and Pharmacokinetics, Bristol-Myers Squibb Company, Syracuse, New York 13221-4755.

SO JOURNAL OF CLINICAL PHARMACOLOGY, (1993). Vol. 33, No. 10, pp. 912-7. Journal code: HT9. ISSN: 0091-2700.

CY United States

DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)

FS MED; Priority Journals

LA English

OS MEDLINE 94043874

EM 199402

AB The steady-state pharmacokinetics of **didanosine** (**DDI**) and **ketoconazole** (KET) were evaluated when the agents were administered alone or concurrently to patients seropositive for the human immunodeficiency virus. Using a randomized, three-way crossover design, multiple oral doses of **DDI** (375 mg twice daily for 4 days), KET (200 mg daily for 4 days) or the combination were administered under fasting conditions. When **DDI** and KET were coadministered, KET was given 2 hours before the morning dose of **didanosine**. Serial blood samples and total urine output were a collected after the administration of a final single dose on day 5 of each treatment session. Samples were analyzed using high-pressure liquid chromatography (HPLC)/ultraviolet (UV) or fluorescence methods specific for unchanged **DDI** (plasma and urine) or KET (plasma only). Pharmacokinetic parameters were calculated using noncompartmental methods. The average

DDI maximum peak plasma concentration (Cmax) value at steady state was significantly less when **DDI** was administered with KET (1836 ng/mL) than when **DDI** was administered alone (2094 ng/mL), although the magnitude of the decrease was only 12%. **Didanosine** area under the curve (AUC(0-tau)) for the combination (2872 hr.ng/mL) was 8% less than when **DDI** was given alone (3107 hr.ng/mL); the difference was not significant. There were no significant differences among the other evaluated parameters (time to reach peak concentration [tmax], half-life [t1/2], renal clearance [CLR], or urinary recovery [UR]) between the two **DDI** treatments. There were no significant differences among any of the pharmacokinetic parameters between the two KET treatments.(ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Comparative Study; Human; Male
Administration, Oral
Adult
Didanosine: AD, administration & dosage
***Didanosine**: PK, pharmacokinetics
Drug Therapy, Combination
Half-Life
*HIV Seropositivity: ME, metabolism
Ketoconazole: AD, administration & dosage
***Ketoconazole**: PK, pharmacokinetics
Specimen Handling

RN **65277-42-1 (Ketoconazole)**; 69655-05-6 (**Didanosine**)

L164 ANSWER 16 OF 23 AIDSLINE
AN 1993:15211 AIDSLINE
DN ICA9-93334958
TI Aspergillus-sinusitis in AIDS with rapid invasion of the orbita and the brain.
AU Schnutgen M; Hohler T; Mayet W J; Meyer zum Buschenfelde K H
CS I. Med. Dept., Univ. of Mainz, Germany.
SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 370 (Abstract No. PO-B09-1406).
CY GERMANY: Germany, Federal Republic of
DT (MEETING ABSTRACTS)
FS ICA9
LA English
EM 199311
AB INTRODUCTION: Aspergillus-infections are a rare complication in the course of the acquired immunodeficiency syndrome. Recently there has been a number of case reports describing invasive pulmonary aspergillosis as the most common organ involvement of this fungal infection. We would like to report the unusual case of an aspergillus-sinusitis complicated by orbital and intracranial invasion. CASE REPORT: A 36-year old homosexual man with AIDS was referred to our hospital because of an exophthalmus of the right eye accompanied by swelling and redness of the upper eyelid. The HIV-infection had been diagnosed in 1988. Subsequently he had suffered from cytomegalovirus-retinitis and a cerebral toxoplasmosis, for which he was treated with gancyclovir and pyrimethamine respectively. This treatment was complicated by repeated drops of neutrophil count. Because of recurrent episodes of fever due to an atypical mycobacterial infection he had received oral corticosteroids for the last year (50 mg/d). The computed tomography scan showed a mass extending from the right maxillary sinus to the right frontal sinus, invading the adjacent bones and the retroorbital space. A biopsy specimen revealed septate hyphae resembling aspergillus and necrotic tissue. Despite therapy with amphotericin B and itraconazole the patient died a few weeks later because of intracranial involvement due to the invasive aspergillosis. DISCUSSION: There have been only very few reports in the literature describing the aspergillus

infections of the sinuses and the orbita. To our knowledge this is the first case of invasive aspergillus-sinusitis demonstrating the destructive character of the disease by rapidly progressive invasion of the orbita, frontal sinus and the brain. Despite of the well known risk factors for invasive aspergillosis like neutropenia and corticosteroid use, our patient had received gancyclovir treatment for the last year. The increasing use of cytotoxic drugs like gancyclovir and **AZT** in the course of HIV-infections will put the patients at higher risks of fungal complications. In these cases otherwise common affections like sinusitis might be caused by pathogens like aspergillus and have a rapid and deleterious course.

CT Check Tags: Case Report; Human; Male
Adult
Amphotericin B: TU, therapeutic use
Antifungal Agents: TU, therapeutic use
Aspergillosis: CO, complications
Aspergillosis: DT, drug therapy
*Aspergillosis: PP, physiopathology
AIDS-Related Opportunistic Infections: DI, diagnosis
AIDS-Related Opportunistic Infections: DT, drug therapy
*AIDS-Related Opportunistic Infections: PP, physiopathology
Biopsy
Brain Diseases: CO, complications
Brain Diseases: DI, diagnosis
*Brain Diseases: PP, physiopathology
Drug Therapy, Combination
Eye Infections, Fungal: CO, complications
Eye Infections, Fungal: DT, drug therapy
*Eye Infections, Fungal: PP, physiopathology
Homosexuality
Ketoconazole: AA, analogs & derivatives
Ketoconazole: TU, therapeutic use
Sinusitis: CO, complications
Sinusitis: DT, drug therapy
Sinusitis: PP, physiopathology
Tomography, X-Ray Computed

RN 1397-89-3 (Amphotericin B); **65277-42-1 (Ketoconazole)**; 84625-61-6 (Itraconazole)

CN 0 (Antifungal Agents)

L164 ANSWER 17 OF 23 AIDSLINE

AN 1993:12523 AIDSLINE

DN ICA9-93335768

TI **Zinc** therapy in HIV infected subjects.

AU Ancarani F; Veccia S; Giacometti A; Mocchegiani E; Marcellini M; Scalise G

CS Inst. of Infectious Diseases, University of Ancona, Italy.

SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 493 (Abstract No. PO-B28-2150).

CY GERMANY: Germany, Federal Republic of

DT (CLINICAL TRIAL)
(MEETING ABSTRACTS)
(RANDOMIZED CONTROLLED TRIAL)

FS ICA9

LA English

EM 199311

AB Seric **zinc** and active thymic hormone++ ++thymulin (FTS) reduction was shown in advanced HIV infection. We studied the short term effects of oral **zinc** administration in asymptomatic HIV infected subjects. 25 subjects with CD4 < 500/ml treated with **AZT** longer than 3 months, were evaluated. 15 of them were randomized to assume 200

mg/die of **zinc** sulphate per os for 1 month (Group A), the other 10 were considered as controls (Group B). Seric **zinc** and FTS were evaluated monthly for 3 times before and after randomization. RESULTS: medium seric **zinc** before randomization was 72.7 mcg/dl (SD +/- 14.5). Group A subjects showed a statistically significative improvement of seric **zinc**: 89.1 (SD +/- 21) and 88.2 (SD +/- 36.3) mcg/dl 15 and 30 days after therapy respectively. Basal seric FTS had a low saturation: 1/4.5 ratio of active/total thymulin (log -2). After 1 month of **zinc** therapy there was an improvement of active thymulin to 3 (log -2). Group A subjects showed also an increase of total lymphocytes. CD4 and CD8 cells. All these effects disappeared 1, 2 months after therapy discontinuation. CONCLUSIONS: asymptomatic HIV infected subjects with CD4 < 500/ml have low levels of seric **zinc** and active FTS. Oral administration of 200 mg/die of **zinc** sulphate improves these parameters, yet below physiologic levels, and mildly increases total lymphocytes and T subpopulations. Our results confirm the immunostimulant effect in T cells of oral **zinc** administration in HIV infected people. It seems reasonable to propose a **zinc** therapy for longer periods and in different doses to evaluate middle and long term effects.

CT Check Tags: Human
*Adjuvants, Immunologic: TU, therapeutic use
Administration, Oral
Combined Modality Therapy
CD4-Positive T-Lymphocytes
Drug Therapy, Combination
HIV Infections: BL, blood
HIV Infections: DT, drug therapy
*HIV Infections: TH, therapy
Leukocyte Count
*Sulfates: TU, therapeutic use
Thymic Factor, Circulating: DF, deficiency
Zidovudine: TU, therapeutic use
Zinc: BL, blood
Zinc: DF, deficiency
***Zinc**: TU, therapeutic use
RN 30516-87-1 (**Zidovudine**); **7440-66-6 (Zinc)**; 7733-02-0 (**Zinc** Sulfate); 78922-62-0 (Thymic Factor, Circulating)
CN 0 (Adjuvants, Immunologic); 0 (Sulfates)

L164 ANSWER 18 OF 23 AIDSLINE
AN 1993:6608. AIDSLINE
DN MED-93216744
TI Antiviral phospholipids. Anti-HIV drugs conjugated to the glycerobackbone of phospholipids.
AU Pidgeon C; Markovich R J; Liu M D; Holzer T J; Novak R M; Keyer K A
CS Department of Medicinal Chemistry and Pharmacognosy, School of Pharmacy, Purdue University, West Lafayette, Indiana 47907.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1993). Vol. 268, No. 11, pp. 7773-8. Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals; Cancer Journals
LA English
OS MEDLINE 93216744
EM 199307
AB Heteroatom fatty acid analogs of myristic acid containing oxygen or sulfur substituted for the alkyl methylene groups inhibit replication of the human immunodeficiency virus (HIV) in infected cells by acting as

alternative substrates during the viral protein myristoylation event. In this class of compounds, 12-methoxydodecanoic acid is the most potent compound but is approximately 10(3)-fold less active than azidothymidine. The antiviral activity of 12-methoxydodecanoic acid can be enhanced > 40-fold by preparing L-alpha-phosphatidylethanolamine containing 12-methoxydodecanoic acid in both alkyl chains. In addition, the diacylated L-alpha-phosphatidylcholine analog containing 12-methoxydodecanoic acid in both alkyl chains (i) has a 15-fold better antiviral selectivity, (ii) is 7-fold more potent, and (iii) is 10-100-fold more **synergistic** with azidothymidine than 12-methoxydodecanoic acid. Because of potent **synergism**, the antiviral selectivity of the diacylated L-alpha-phosphatidylcholine analog is > 10(4) when coadministered with azidothymidine. Phospholipid conjugates are chiral at the C-2 carbon of the glycerol backbone and most interesting is the observation that both the D- and L-isomers of phosphatidylcholine, phosphatidylglycerol, phosphatidic acid, and **phosphatidylserine** have approximately equal antiviral activity. Phospholipase A2 stereospecifically hydrolyzes only the L isomer of phospholipids and similar activity for both the D- and L- phospholipid isomers suggests that phospholipase A2 is not the rate-limiting enzyme for release of the drugs in vivo.

CT Check Tags: Comparative Study; Human
Antiviral Agents: BL, blood
Antiviral Agents: CS, chemical synthesis
*Antiviral Agents: PD, pharmacology
Cell Line
Cells, Cultured
Drug Design
Drug **Synergism**
Half-Life
*HIV-1: DE, drug effects
HIV-1: EN, enzymology
HIV-1: PH, physiology
Isomerism
Laurates: PD, pharmacology
Leukocytes, Mononuclear: EN, enzymology
Phospholipids: BL, blood
Phospholipids: CS, chemical synthesis
*Phospholipids: PD, pharmacology
RNA-Directed DNA Polymerase: ME, metabolism
Structure-Activity Relationship
*Virus Replication: DE, drug effects
Zidovudine: PD, pharmacology

RN 30516-87-1 (**Zidovudine**); 92169-28-3 (12-methoxydodecanoate)

CN EC 2.7.7.- (HIV-1 Reverse Transcriptase); EC 2.7.7.49 (RNA-Directed DNA Polymerase); 0 (Antiviral Agents); 0 (Laurates); 0 (Phospholipids)

L164 ANSWER 19 OF 23 AIDSLINE

AN 1992:15347 AIDSLINE

DN ICA8-92401011

TI Preliminary results of a broad-based primary prophylaxis phase I study in HIV-infected persons wtih CD4 counts less than or equal to 200/mm3.

AU Weiser J; Rosenstein H; Melroe H; Sullivan C; Henry K

CS Abbott Northwestern Hospital, Mpls, MN.

SO Int Conf AIDS, (1992). Vol. 8, No. 2, pp. B133 (Abstract No. PoB 3278).

CY Netherlands

DT (MEETING ABSTRACTS)

FS ICA8

LA English

EM 199212

AB OBJECTIVES: To assess the feasibility, compliance, and safety of a combination of antimicrobial drugs for the simultaneous primary prevention of herpes group, fungal, Pneumocystis, Mycobacterium avium-intracellulare, and toxoplasmosis-related opportunistic infections in HIV-infected persons with CD4 less than or equal to 200/mm3. METHODS: Beginning in 8/91, 23 HIV-infected persons (all with CD4 counts less than or equal to 200; mean = 96; 18 were CDC Group III and 5 had AIDS; 22 men, 1 woman; mean age 37; anti-HIV regimen was: ZDV, 14;**ddI**, 1; **ddC**, 2; **AZT/ddC**, 2; 1 **ddI** ACTG Protocol) were enrolled in an open-label primary prophylaxis protocol and started on the following drugs: acyclovir 3200mg/day, fluconazole 100mg/day (**ketoconazole** if intolerant), ciprofloxacin 500mg/day (3 patients on rifabutin protocol 027), and TMP/SMX 1 DS/day (if intolerant then dapsone 100 mg/day or aerosolized pentamadine 300mg/4 weeks). Patients were evaluated monthly for compliance, tolerance, laboratory studies and HIV-related events. RESULTS: Twenty-one of 23 are currently active (mean time = 4.3 months, range 1-7 months). There have been two withdrawals (1 due to adverse side effects and 1 for personal/health reasons) and eight episodes of possible study drug-related adverse reactions in 5 patients (ciprofloxacin (2); T/S (3); and 3 multi-system episodes in 1 patient that could not be assigned to a single drug). Monthly laboratory studies have revealed no significant changes in hematologic, liver, or renal function. There has been one episode of of an AIDS-defining OI (MAI infection). Px acceptance of the study regimen has been good. Compliance rates with the drug regimens were high based on the monthly pill counts (Acyclovir 84%, fluconazole 93%, TMP/SMX 92%, and ciprofloxacin 92%). CONCLUSIONS: With the demonstrated efficacy of prophylaxis for AIDS-related PCP, there is much interest in the development of prophylaxis for other AIDS related OIs. Many efficacy trials addressing this issue are underway. This pilot study demonstrates that the polypharmacologic regimens that are evolving can be accepted by patients with tolerable levels of adverse events and high compliance rates. Further study of our cohort and larger studies will need to address efficacy issues.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Acyclovir: TU, therapeutic use
Adult
*Anti-Infective Agents: TU, therapeutic use
Antitubercular Agents: TU, therapeutic use
Ciprofloxacin: TU, therapeutic use
CD4-Positive T-Lymphocytes: IM, immunology
Drug Evaluation
Drug Therapy, Combination
Fluconazole: TU, therapeutic use
HIV Infections: CO, complications
*HIV Infections: DT, drug therapy
HIV Infections: IM, immunology
Leukocyte Count
Opportunistic Infections: CO, complications
Opportunistic Infections: IM, immunology
*Opportunistic Infections: PC, prevention & control
Rifamycins: TU, therapeutic use
Trimethoprim-Sulfamethoxazole Combination: TU, therapeutic use
Zalcitabine: TU, therapeutic use
Zidovudine: TU, therapeutic use

RN 30516-87-1 (**Zidovudine**); 59277-89-3 (Acyclovir); 72559-06-9 (Rifabutin); 7481-89-2 (**Zalcitabine**); 8064-90-2 (Trimethoprim-Sulfamethoxazole Combination); 85721-33-1 (Ciprofloxacin); 86386-73-4 (Fluconazole)

CN 0 (Anti-Infective Agents); 0 (Antitubercular Agents); 0 (Rifamycins)

L164 ANSWER 20 OF 23 AIDSLINE
AN 1991:3035 AIDSLINE
DN MED-91117576
TI Mother to child transmission of human immunodeficiency virus 1 infection despite **zidovudine** therapy from 18 weeks of gestation.
AU Barzilai A; Sperling R S; Hyatt A C; Wedgwood J F; Reidenberg B E; Hodes D S
CS Department of Pediatrics and Obstetrics, Mount Sinai School of Medicine, New York, NY 10029.
NC UO1-AI-27554 (NIAID)
SO PEDIATRIC INFECTIOUS DISEASE JOURNAL, (1990). Vol. 9, No. 12, pp. 931-3. Journal code: OXJ. ISSN: 0891-3668.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 91117576
EM 199105
CT Check Tags: Case Report; Female; Human; Support, U.S. Gov't, P.H.S.
Acyclovir: TU, therapeutic use
Adult
*Diseases in Twins
Drug Therapy, Combination
HIV Infections: DT, drug therapy
*HIV Infections: TM, transmission
*HIV-1
Infant, Newborn
Infant, Premature, Diseases
Ketoconazole: TU, therapeutic use
Patient Compliance
Pregnancy
*Pregnancy Complications, Infectious: DT, drug therapy
***Zidovudine**: TU, therapeutic use
RN 30516-87-1 (**Zidovudine**); 59277-89-3 (Acyclovir); **65277-42-1 (Ketoconazole)**

L164 ANSWER 21 OF 23 AIDSLINE
AN 1990:10300 AIDSLINE
DN ICA5-00178689
TI Retreatment of syphilis in HIV positive patients.
AU Phillip H; Harris J R; Goldmeier D
CS The Praed Street Clinic, St Mary's Hospital, London, W2 1NY, United Kingdom.
SO Int Conf AIDS, (1989). Vol. 5, pp. 361 (Abstract No. W.B.P.58). ISBN: 0-662-56670-X.
CY Canada
DT (MEETING ABSTRACTS)
(CLINICAL TRIAL)
FS ICA5
LA English
EM 199009
AB OBJECTIVE: Treponemes can persist in the CNS following standard treatment of early syphilis with benzathine or **procaine** penicillin. Approximately 50% of homosexuals with AIDS have had syphilis, and it is possible that persisting treponemal infection contributes to the neurological manifestations of AIDS. We are performing a trial to assess the benefits of retreatment with an antibiotic regime that achieves good

CNS penetration. METHODS: A double-blind placebo controlled trial using amoxicillin 3 g bd/probenecid 500 mg bd for HIV positive patients previously treated for syphilis. All patients have CDC stage 4 disease. They are assessed over 6 months with neuropsychiatric tests, neurological examination and serology. RESULTS: Nineteen patients have been treated so far. One withdrew due to penicillin allergy, 2 because of admission to hospital. Four patients stopped after 2 weeks because of minor reactions. Twelve completed the 3 week course. So far no significant difference between the treatment and placebo groups has emerged. CONCLUSIONS: These are small numbers of patients but the results of long term follow up will yield more information. Probenecid increases the half-life of **Zidovudine**. This has prevented use of the trial treatment in patients taking **Zidovudine**, until the safety of such a combination is assessed. The amoxicillin and probenecid regime may be useful for the initial treatment of syphilis in HIV positive patients.

CT Check Tags: Human
*Amoxicillin: TU, therapeutic use
Clinical Trials
Double-Blind Method
Drug Therapy, Combination
*HIV Infections: CO, complications
Neurosyphilis: CO, complications
*Neurosyphilis: DT, drug therapy
Placebos
Probenecid: AD, administration & dosage
*Probenecid: TU, therapeutic use
Zidovudine: AD, administration & dosage

RN 26787-78-0 (Amoxicillin); 30516-87-1 (**Zidovudine**); 57-66-9 (Probenecid)

CN 0 (Placebos)

L164 ANSWER 22 OF 23 AIDSLINE

AN 1990:7926 AIDSLINE

DN ICA5-00257189

TI EFFICACY AND SAFETY OF **KETOCONAZOLE** IN HIV INFECTED INFANTS WITH mucocutaneous candidiasis.

AU LeMay M D; Cooper E R; Patel D K; Pelton S I

CS Boston City Hospital and Boston University School of Medicine, Boston, Massachusetts, USA.

SO Int Conf AIDS, (1989). Vol. 5, pp. 496 (Abstract No. B.591). ISBN: 0-662-56670-X.

CY Canada

DT (MEETING ABSTRACTS)

FS ICA5

LA English

EM 199009

AB Mucocutaneous candidiasis is a frequent opportunistic infection in children with HIV disease and associated with significant morbidity (pain, poor feeding, failure to thrive). Recommended therapies such as Nystatin and gentian violet have not been efficacious in immunocompromised hosts with moderate to severe candidiasis. We treated 4 infants, ages 1 to 8 mos. with a **Ketoconazole** suspension (prepared by pharmacy) of 3 mg/kg q 12 h for moderate to severe thrush (3 patients) which involved buccal mucosa, tongue and palate and was associated with poor feeding and weight loss. All had failed a minimum of 7 days of Nystatin plus gentian violet. All 3 cleared on **Ketoconazole** in 3-5 days. 2/3 had recurrence when therapy was discontinued which necessitated "prophylactic" administration of 3 mg/kg/day for 3 and 10 mos. respectively. 1 patient (8 mos.) was treated for monilial dermatitis which had failed topical

therapy. The rash cleared after 10 days of treatment. All patients tolerated **Ketoconazole** well. All children had pre and post treatment evaluation of liver function. No adverse effects were observed. Specifically 1 infant (P2 F1) 4 mos. of age received **Ketoconazole** and **Zidovudine** concurrently for 3 mos. Pre therapy LFTs demonstrate moderate hepatocellular injury (SGOT 390, SGPT 149, Bili 7.3). LFTs progressively return to normal values (SGOT79, SPGT 50, Bili .7) over a 3 mos. course while on both medications. We believe **Ketoconazole** is a safe and effective therapy of mucocutaneous candidiasis. More information is needed about its concurrent use with **Zidovudine** and its use in children with evidence of hepatocellular dysfunction.

CT Check Tags: Human
Candidiasis, Chronic Mucocutaneous: CO, complications
*Candidiasis, Chronic Mucocutaneous: DT, drug therapy
Drug Therapy, Combination
Drug Tolerance
*HIV Infections: CO, complications
Infant
Ketoconazole: AE, adverse effects
***Ketoconazole**: PD, pharmacology
Ketoconazole: TU, therapeutic use
Nystatin: TU, therapeutic use
Zidovudine: TU, therapeutic use

RN 1400-61-9 (Nystatin); 30516-87-1 (**Zidovudine**); **65277-42-1 (Ketoconazole)**

L164 ANSWER 23 OF 23 AIDSLINE
AN 1990:1612 AIDSLINE
DN MED-90085805
TI Inhibition of human immunodeficiency virus (HIV-1) infection by diphenylhydantoin (dilantin) implicates role of cellular calcium in virus life cycle.
AU Cloyd M W; Lynn W S; Ramsey K; Baron S
CS Department of Microbiology, University of Texas Medical Branch Galveston 77550.
NC AI-25722 (NIAID)
SO VIROLOGY, (1989). Vol. 173, No. 2, pp. 581-90.
Journal code: XEA. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals; Cancer Journals
LA English
OS MEDLINE 90085805
EM 199003
AB Details of the molecular interactions between human immunodeficiency virus (HIV-1) and its host cell during the infection process are not entirely clear. Building on recent reports by Lehr and Zimmer (1986, DMW 111, 1001-1002) that the membrane-reactive, anti-epileptic drug diphenylhydantoin (dilantin or **phenytoin**) (PHT) inhibited binding of HIV to lymphocytes, we hypothesized that understanding the relevant effects of this drug on cells may shed light on aspects of HIV-1 infection. We found that PHT inhibited, in a dose-dependent manner, de novo infection of various T-cell lines as well as a monocytic cell line. Moderate inhibition of HIV-1 infection was observed with drug concentrations that are therapeutic in vivo for epilepsy (approximately 20 micrograms/ml), and no concentrations used induced deleterious effects on cell growth or viability. Surprisingly, treatment of chronically infected H9 cells reduced HIV p24 expression within 1-6 weeks according to dose. This apparent induction into latency was not inhibited by cotreatment of

the chronically infected cells with 5-azacytidine, which indicated that PHT was not inducing latency by induction of methylation of the viral DNA. Flow cytometric analysis demonstrated that PHT did not significantly reduce cell-surface expression of CD4. The possibility remained that the drug inhibited HIV infection due to its known effects on calcium-dependent cellular processes. Subsequent measurements of intracellular calcium demonstrated that an increase of [Ca2+]i occurred at least 24 hr postinfection, prior to synthesis of detectable viral structural protein p24, and that this virus-induced increase in [Ca2+]i was not due to binding of HIV to the cell. This HIV-induced rise in [Ca2+]i was significantly inhibited by PHT. PHT demonstrated variable inhibitory effects on infection of normal PHA-stimulated PBLs cultured in vitro, but it was **synergistic** to low-dose **AZT** (0.01 microgram/ml) in inhibiting infection of cell lines. Because of the known inhibitory effects of PHT on calcium-dependent biochemical processes in the cell, inhibition of HIV-1 infection by PHT suggests that calcium may play a role in HIV infection and maintenance. The drug may also be a candidate therapy for individuals infected with HIV.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Calcium: ME, metabolism
Cell Line
*CD4-Positive T-Lymphocytes: MI, microbiology
Drug **Synergism**
*HIV-1: DE, drug effects
HIV-1: PH, physiology
*Monocytes: MI, microbiology
***Phenytoin**: PD, pharmacology
Virus Replication: DE, drug effects
Zidovudine: PD, pharmacology

RN 30516-87-1 (**Zidovudine**); **57-41-0 (Phenytoin)**;
7440-70-2 (Calcium)

=> d all tot l165

L165 ANSWER 1 OF 20 AIDSLINE
AN 1999:3050 AIDSLINE
DN MED-99028712
TI **Ritonavir**. Clinical pharmacokinetics and interactions with other anti-HIV agents.
AU Hsu A; Granneman G R; Bertz R J
CS Abbott Laboratories, Abbott Park, Illinois, USA. Ann.Hsu@Abbott.com
SO CLINICAL PHARMACOKINETICS, (1998). Vol. 35, No. 4, pp. 275-91.
Journal code: DG5. ISSN: 0312-5963.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
FS MED; Priority Journals
LA English
OS MEDLINE 99028712
EM 199903
AB **Ritonavir** is 1 of the 4 potent synthetic HIV protease inhibitors, approved by the US Food and Drug Administration (FDA) between 1995 and 1997, that have revolutionised HIV therapy. The extent of oral absorption is high and is not affected by food. Within the clinical concentration range, **ritonavir** is approximately 98 to 99% bound to plasma proteins, including albumin and alpha 1-acid glycoprotein. Cerebrospinal fluid (CSF) drug concentrations are low in relation to total plasma concentration. However, parallel decreases in the viral burden have

been observed in the plasma, CSF and other tissues. **Ritonavir** is primarily metabolised by cytochrome P450 (CYP) 3A isozymes and, to a lesser extent, by CYP2D6. Four major oxidative metabolites have been identified in humans, but are unlikely to contribute to the antiviral effect. About 34% and 3.5% of a 600 mg dose is excreted as unchanged drug in the faeces and urine, respectively. The clinically relevant t1/2 beta is about 3 to 5 hours. Because of autoinduction, plasma concentrations generally reach steady state 2 weeks after the start of administration. The pharmacokinetics of **ritonavir** are relatively linear after multiple doses, with apparent oral clearance averaging 7 to 9 L/h. In vitro, **ritonavir** is a potent inhibitor of CYP3A. In vivo, **ritonavir** significantly increases the AUC of drugs primarily eliminated by CYP3A metabolism (e.g. clarithromycin, **ketoconazole**, rifabutin, and other HIV protease inhibitors, including **indinavir**, **saquinavir** and **nelfinavir**) with effects ranging from an increase of 77% to 20-fold in humans. It also inhibits CYP2D6-mediated metabolism, but to a significantly lesser extent (145% increase in desipramine AUC). Since **ritonavir** is also an inducer of several metabolising enzymes [CYP1A4, glucuronosyl transferase (GT), and possibly CYP2C9 and CYP2C19], the magnitude of drug interactions is difficult to predict, particularly for drugs that are metabolised by multiple enzymes or have low intrinsic clearance by CYP3A. For example, the AUC of CYP3A substrate methadone was slightly decreased and alprazolam was unaffected. **Ritonavir** is minimally affected by other CYP3A inhibitors, including **ketoconazole**. Rifampicin (rifampin), a potent CYP3A inducer, decreased the AUC of **ritonavir** by only 35%. The degree and duration of suppression of HIV replication is significantly correlated with the plasma concentrations. Thus, the large increase in the plasma concentrations of other protease inhibitors when coadministered with **ritonavir** forms the basis of rational dual protease inhibitor regimens, providing patients with 2 potent drugs at significantly reduced doses and less frequent dosage intervals. **Combination** treatment of **ritonavir** with **saquinavir** and **indinavir** results in potent and sustained clinical activity. Other important factors with **combination** regimens include reduced interpatient variability for high clearance agents, and elimination of the food effect on the bioavailibility of **indinavir**.

CT Check Tags: Animal; Human
Anti-HIV Agents: PD, pharmacology
*Anti-HIV Agents: PK, pharmacokinetics
Drug Interactions
HIV Protease Inhibitors: PD, pharmacology
*HIV Protease Inhibitors: PK, pharmacokinetics
Ritonavir: PD, pharmacology
***Ritonavir**: PK, pharmacokinetics

CN 0 (Anti-HIV Agents); 0 (HIV Protease Inhibitors); 0 (**Ritonavir**)

L165 ANSWER 2 OF 20 AIDSLINE
AN 1997:17162 AIDSLINE
DN MED-97253549
TI Determination of an in vivo metabolite of a human immunodeficiency virus protease-inhibitor in human plasma by high-performance liquid chromatography with tandem mass spectrometry.
AU Woolf E; Haddix H M; Matuszewski B
CS Merck Research Laboratories, Department of Drug Metabolism, PA 19486, USA.
SO JOURNAL OF CHROMATOGRAPHY. A, (1997). Vol. 762, No. 1-2, pp. 311-9.
Journal code: BXJ.
CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 97253549
EM 199708
AB A method for the determination of a metabolic of the human immunodeficiency virus protease inhibitor **indinavir**, in human plasma is described. Isolation of the analyte and the internal standard from plasma was achieved via liquid-liquid extraction with a mixture of isopropanol-chloroform (5:95, v/v). The analytes were chromatographed under reversed-phase conditions on a Waters Symmetry C, column. A Sciex API III+ tandem mass spectrometer equipped with a heated nebulizer was used as a detector and was operated in the positive ion mode. Multiple reaction monitoring using the precursor-->production **combinations** of m/z, 523.4-->273.4 and 512.4-->345.2 was used to quantify analyte and internal standard, respectively. The method was validated in the concentration range of 5-500 ng/ml plasma with adequate assay precision and accuracy. The assay was used to analyze samples collected during drug interaction studies of **indinavir**.
CT Check Tags: Comparative Study; Human
Antifungal Agents: AD, administration & dosage
Antifungal Agents: PK, pharmacokinetics
*Chromatography, High Pressure Liquid: MT, methods
Circadian Rhythm
HIV Protease Inhibitors: AD, administration & dosage
*HIV Protease Inhibitors: BL, blood
HIV Protease Inhibitors: CH, chemistry
HIV Protease Inhibitors: PK, pharmacokinetics
Indinavir: AD, administration & dosage
***Indinavir**: BL, blood
Indinavir: CH, chemistry
Indinavir: PK, pharmacokinetics
Ketoconazole: AD, administration & dosage
Ketoconazole: PK, pharmacokinetics
Linear Models
Reproducibility of Results
Sensitivity and Specificity
*Spectrum Analysis, Mass: MT, methods
RN 150378-17-9 (**Indinavir**); **65277-42-1 (Ketoconazole)**
CN 0 (Antifungal Agents); 0 (HIV Protease Inhibitors)

L165 ANSWER 3 OF 20 AIDSLINE
AN 1997:15473 AIDSLINE
DN MED-97239297
TI Protease inhibitors in patients with HIV disease. Clinically important pharmacokinetic considerations.
AU Barry M; Gibbons S; Back D; Mulcahy F
CS Department of Pharmacology and Therapeutics, University of Liverpool, England.
SO CLINICAL PHARMACOKINETICS, (1997). Vol. 32, No. 3, pp. 194-209. Journal code: DG5. ISSN: 0312-5963.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
FS MED; Priority Journals
LA English
OS MEDLINE 97239297
EM 199707

AB Since its introduction in 1987, **zidovudine** monotherapy has been the treatment of choice for patients with HIV infection. Unfortunately it has been established that the beneficial effects of **zidovudine** are not sustained due to the development of resistant viral strains. This has led to the strategy of **combination** therapy, and in 1995 treatment with **zidovudine** plus **didanosine**, or **zidovudine** plus **zalcitabine**, was demonstrated to be more effective than **zidovudine** monotherapy in preventing disease progression and reducing mortality in patients with HIV disease. Recent work demonstrates an even greater antiviral effect from triple therapy with 2 nucleosides, **zidovudine** plus **zalcitabine** with the addition of **saquinavir**, a new protease inhibitor drug. The HIV protease enzyme is responsible for the post-translational processing of gag and gag-pol polyprotein precursors, and its inhibition by drugs such as **saquinavir**, **ritonavir**, **indinavir** and VX-478 results in the production of non-infectious virions. As resistance may also develop to the protease inhibitors they may be used in **combination**, and future strategies may well include quadruple therapy with 2 nucleoside analogues plus 2 protease inhibitors. Administration of protease inhibitors alone or in **combination** with other drugs does raise a number of important pharmacokinetic issues for patients with HIV disease. Some protease inhibitors (e.g. **saquinavir**) have kinetic profiles characterised by reduced absorption and a high first pass effect, resulting in poor bioavailability which may be improved by administrating with food. Physiological factors including achlorhydria, malabsorption and hepatic dysfunction may influence the bioavailability of protease inhibitors in HIV disease. Protease inhibitors are very highly bound to plasma proteins (> 98%), predominantly to alpha 1-acid glycoprotein. This may influence their antiviral activity in vitro and may also predispose to plasma protein displacement interactions. Such interactions are usually only of clinical relevance if the metabolism of the displaced drug is also inhibited. This is precisely the situation likely to pertain to the protease inhibitors, as **ritonavir** may displace other protease inhibitor drugs, such as **saquinavir**, from plasma proteins and inhibit their metabolism. Protease inhibitors are extensively metabolised by the cytochrome P450 (CYP) enzymes present in the liver and small intestine. In vitro studies suggest that the most influential CYP isoenzyme involved in the metabolism of the protease inhibitors is CYP3A, with the isoforms CYP2C9 and CYP2D6 also contributing. **Ritonavir** has an elimination half-life (t1/2 beta) of 3 hours, **indinavir** 2 hours and **saquinavir** between 7 and 12 hours. Renal elimination is not significant, with less than 5% of **ritonavir** and **saquinavir** excreted in the unchanged form. As patients with HIV disease are likely to be taking multiple prolonged drug regimens this may lead to drug interactions as a result of enzyme induction or inhibition. Recognised enzyme inducers of CYP3A, which are likely to be prescribed for patients with HIV disease, include rifampicin (rifampin) [treatment of pulmonary tuberculosis], rifabutin (treatment and prophylaxis of Mycobacterium avium complex), phenobarbital (phenobarbitone), **phenytoin** and carbamazepine (treatment of seizures secondary to cerebral toxoplasmosis or cerebral lymphoma). These drugs may reduce the plasma concentrations of the protease inhibitors and reduce their antiviral efficacy. If coadministered drugs are substrates for a common CYP enzyme, the elimination of one or both drugs may be impaired. Drugs which are metabolised by CYP3A and are likely to be used in the treatment of patients with HIV disease include the azole antifungals, macrolide antibiotics and dapsone; therefore, protease inhibitors may interact with these drugs. (ABSTRACT TRUNCATED)

CT Check Tags: Human
Anti-HIV Agents: TU, therapeutic use
Biological Availability
Blood Proteins: ME, metabolism
Half-Life
*HIV Infections: DT, drug therapy
HIV Infections: ME, metabolism
Metabolic Clearance Rate
Protease Inhibitors: ME, metabolism
*Protease Inhibitors: PK, pharmacokinetics
*Protease Inhibitors: TU, therapeutic use
Zidovudine: TU, therapeutic use
RN 30516-87-1 (**Zidovudine**)
CN 0 (Anti-HIV Agents); 0 (Blood Proteins); 0 (Protease Inhibitors)

L165 ANSWER 4 OF 20 AIDSLINE
AN 1997:15293 AIDSLINE
DN MED-97180839
TI Selective biotransformation of the human immunodeficiency virus protease inhibitor **saquinavir** by human small-intestinal cytochrome P4503A4: potential contribution to high first-pass metabolism.
AU Fitzsimmons M E; Collins J M
CS Laboratory of Clinical Pharmacology, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, Rockville, MD 20850, USA.
SO DRUG METABOLISM AND DISPOSITION, (1997). Vol. 25, No. 2, pp. 256-66. Journal code: EBR. ISSN: 0090-9556.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 97180839
EM 199707
AB **Saquinavir** is a HIV protease inhibitor used in the treatment of patients with acquired immunodeficiency syndrome, but its use is limited by low oral bioavailability. The potential of human intestinal tissue to metabolize **saquinavir** was assessed in 17 different human small-intestinal microsomal preparations. **Saquinavir** was metabolized by human small-intestinal microsomes to numerous mono- and dihydroxylated species with K(M) values of 0.3-0.5 microM. The major metabolites M-2 and M-7 were single hydroxylations on the octahydro-2-(1H)-isoquinolinyl and (1,1-dimethylethyl)amino groups, respectively. **Ketoconazole** and troleandomycin, selective inhibitors of cytochrome P4503A4 (CYP3A4), were potent inhibitors for all oxidative metabolites of **saquinavir**. The cytochrome P450-selective inhibitors furafylline, fluvoxamine, sulfaphenazole, mephenytoin, quinidine, and chlorzoxazone had little inhibitory effect. All **saquinavir** metabolites were highly correlated with testosterone 6beta-hydroxylation and with each other. Human hepatic microsomes and recombinant CYP3A4 oxidized **saquinavir** to the same metabolic profile observed with human small-intestinal microsomes. **Indinavir**, a potent HIV protease inhibitor and a substrate for human hepatic CYP3A4, was a comparatively poor substrate for human intestinal microsomes and inhibited the oxidative metabolism of **saquinavir** to all metabolites with a Ki of 0.2 microM. In addition, **saquinavir** inhibited the human, small-intestinal, microsomal CYP3A4-dependent detoxication pathway of terfenadine to its alcohol metabolite with a Ki value of 0.7 microM. These data indicate that **saquinavir** is metabolized by human intestinal CYP3A4, that this metabolism may contribute to its poor oral bioavailability, and that

combination therapy with **indinavir** or other protease inhibitors may attenuate its low relative bioavailability.

CT Check Tags: Comparative Study; Human
*Anti-HIV Agents: ME, metabolism
Anti-HIV Agents: PK, pharmacokinetics
Biotransformation
*Cytochrome P-450: ME, metabolism
Drug Interactions
Histamine H1 Antagonists: ME, metabolism
*Hydroxylases: ME, metabolism
*HIV Protease Inhibitors: ME, metabolism
HIV Protease Inhibitors: PK, pharmacokinetics
Indinavir: ME, metabolism
*Intestine, Small: EN, enzymology
Ketoconazole
Microsomes: EN, enzymology
Microsomes, Liver: EN, enzymology
Oxidation-Reduction
***Saquinavir**: ME, metabolism
Saquinavir: PK, pharmacokinetics
Terfenadine: ME, metabolism

RN 127779-20-8 (**Saquinavir**); 150378-17-9 (**Indinavir**); 50679-08-8 (Terfenadine); **65277-42-1 (Ketoconazole)**; 9035-51-2 (Cytochrome P-450)

CN EC 1.14. (Hydroxylases); EC 1.14.99.- (nifedipine oxidase); 0 (Anti-HIV Agents); 0 (Histamine H1 Antagonists); 0 (HIV Protease Inhibitors)

L165 ANSWER 5 OF 20 AIDSLINE
AN 1996:6821 AIDSLINE
DN AIDS-96700971
TI More clinical data on protease inhibitors.
AU Smart T
SO GMHC Treat Issues, (1995). Vol. 9, No. 10, pp. 4-7.
CY United States
DT (NEWSLETTER ARTICLE)
FS AIDS
LA English
EM 199608
AB Clinical information from Abbott Laboratories, Merck, Hoffman-LaRoche, and Agouron is provided on the following protease inhibitors: **ritonavir**, **indinavir** sulfate (Crixivan), **saquinavir**, and Viracept. Overall, the research presented suggests that higher doses of these drugs, and **combinations** with nucleoside analogs, appear to produce more potent and durable antiviral effects than seen in earlier protease inhibitor studies. An update is included on protease inhibitor compassionate use programs on **indinavir**, **saquinavir**, and Viracept; as well as a list of protease drug interactions for **ritonavir** and **indinavir**.

CT Check Tags: Human
*Acquired Immunodeficiency Syndrome: DT, drug therapy
Clinical Trials
CD4 Lymphocyte Count
Drug Resistance, Microbial
HIV: DE, drug effects
HIV: GE, genetics
*HIV Infections: DT, drug therapy
HIV Protease Inhibitors: PD, pharmacology
HIV Protease Inhibitors: PK, pharmacokinetics

*HIV Protease Inhibitors: TU, therapeutic use
Ketoconazole: ME, metabolism
Liver: ME, metabolism
Mutation
Patient Compliance
RN **65277-42-1 (Ketoconazole)**
CN 0 (HIV Protease Inhibitors)

L165 ANSWER 6 OF 20 AIDSLINE
AN 1996:1636 AIDSLINE
DN MED-96142384
TI [Nonketotic hyperglycemic coma induced by somatostatin in an AIDS patient].
Coma hyperglycemique non cetosique induit par la somatostatine chez un patient atteint du SIDA.
AU Vandercam B; Hermans M P; Coumans P; Jacques D; Gala J L; Kolanowski J
CS Departement de Medecine interne, Cliniques Universitaires Saint-Luc, Bruxelles, Belgique.
SO PRESSE MEDICALE, (1995). Vol. 24, No. 30, pp. 1389-90.
Journal code: PMT. ISSN: 0755-4982.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals; Cancer Journals
LA French
SL English
OS MEDLINE 96142384
EM 199604
AB A 33-year-old woman with AIDS was treated with somatostatin (continuous infusion 6 mg/day) for intractable diarrhoea. Improvement was insufficient and the dose was increased to 12 mg/day 5 days later. Hyperosmolar non-ketotic coma occurred two days later (blood glucose 53 mmol/l, bicarbonate 8 mmol/l, pH of arterial blood 7.2). Search for urinary ketones was negative. Klebsiella pneumonia was isolated in the urine sample. Somatostatin was withdrawn and the patient improved with parenteral nutrition and intravenous insulin. Glucose tolerance was verified after recovery and was normal. Somatostatin is known to impair glucose tolerance and as shown in this case should also be recognized as a cause of hyperosmolar non-ketotic coma. Increasing use of somatostatin, particularly in HIV patients often given other hyperglycaemia inducing drugs such as **didanosine**, pentamidine, dapsone, and **phenytoin** should be accompanied with careful monitoring of blood glucose levels.
CT Check Tags: Case Report; Female; Human
*Acquired Immunodeficiency Syndrome: CO, complications
Adult
Antibiotics, **Combined**: TU, therapeutic use
AIDS-Related Opportunistic Infections: DT, drug therapy
AIDS-Related Opportunistic Infections: MI, microbiology
*Diarrhea: DT, drug therapy
Diarrhea: ET, etiology
English Abstract
Hormone Antagonists: AD, administration & dosage
*Hormone Antagonists: AE, adverse effects
Hormone Antagonists: TU, therapeutic use
*Hyperglycemic Hyperosmolar Nonketotic Coma: CI, chemically induced
Klebsiella Infections: CO, complications
Klebsiella Infections: DT, drug therapy
Klebsiella Infections: MI, microbiology
Somatostatin: AD, administration & dosage

*Somatostatin: AE, adverse effects
Somatostatin: TU, therapeutic use
Urinary Tract Infections: CO, complications
Urinary Tract Infections: DT, drug therapy
Urinary Tract Infections: MI, microbiology
RN 51110-01-1 (Somatostatin)
CN 0 (Antibiotics, **Combined**); 0 (Hormone Antagonists)

L165 ANSWER 7 OF 20 AIDSLINE
AN 1996:305 AIDSLINE
DN MED-96085720
TI Micronutrients and HIV-1 disease progression.
AU Baum M K; Shor-Posner G; Lu Y; Rosner B; Sauberlich H E; Fletcher M A; Szapocznik J; Eisdorfer C; Buring J E; Hennekens C H
CS Department of Epidemiology and Public Health, University of Miami School of Medicine, Florida 33101, USA.
NC 1P50MH4255 (NIMH)
KO4HL01862 (NHLBI)
SO AIDS, (1995). Vol. 9, No. 9, pp. 1051-6.
Journal code: AID. ISSN: 0269-9370.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 96085720
EM 199604
AB OBJECTIVE: To determine whether nutritional status affects immunological markers of HIV-1 disease progression. DESIGN: A longitudinal study, to evaluate the relationship between plasma levels of nutrients and CD4 cell counts, along and in **combination** with beta 2-microglobulin (beta 2M; AIDS index) over an 18-month follow-up. METHODS: Biochemical measurements of nutritional status including plasma proteins, **zinc**, iron and vitamins B1, B2, B6, B12 (cobalamin), A, E, C and folate and immunological markers [lymphocyte subpopulations (CD4) and beta 2M] were obtained in 108 HIV-1-seropositive homosexual men at baseline and over three 6-month time periods. Changes in nutrient status (e.g., normal to deficient, deficient to normal), were compared with immunological parameters in the same time periods using an autoregressive model. RESULTS: Development of deficiency of vitamin A or vitamin B12 was associated with a decline in CD4 cell count (P = 0.0255 and 0.0377, respectively), while normalization of vitamin A, vitamin B12 and **zinc** was associated with higher CD4 cell counts (P = 0.0492, 0.0061 and 0.0112, respectively). These findings were largely unaffected by **zidovudine** use. For vitamin B12, low baseline status significantly predicted accelerated HIV-1 disease progression determined by CD4 cell count (P = 0.041) and the AIDS index (P = 0.005). CONCLUSIONS: These data suggest that micronutrient deficiencies are associated with HIV-1 disease progression and raise the possibility that normalization might increase symptom-free survival.
CT Check Tags: Human; Male; Support, U.S. Gov't, P.H.S.
beta 2-Microglobulin: ME, metabolism
Adult
Blood Proteins: ME, metabolism
*CD4 Lymphocyte Count
Disease Progression
Follow-Up Studies
*HIV Infections: IM, immunology
*HIV-1: IM, immunology
Longitudinal Studies

Middle Age
*Nutritional Status
*Trace Elements: BL, blood
Vitamin A Deficiency: IM, immunology
Vitamin B 12 Deficiency: IM, immunology
*Vitamins: BL, blood
Zinc: BL, blood
Zinc: DF, deficiency
RN **7440-66-6 (Zinc)**
CN 0 (beta 2-Microglobulin); 0 (Blood Proteins); 0 (Trace Elements); 0 (Vitamins)

L165 ANSWER 8 OF 20 AIDSLINE
AN 1995:8721 AIDSLINE
DN AIDS-95920017
TI HIV-1 integrase inhibitors: discovery, structure-activity, inhibition mechanisms, selectivity.
AU Pommier Y; Mazumder A; Kohn K W
CS Laboratory of Molecular Pharmacology, National Cancer Institute, NIH, Bethesda, MD.
SO NIH Conf Retroviral Integrase, (1995). pp. (Session III, speakers' Abstracts - unpaged).
CY United States
DT (MEETING ABSTRACTS)
FS AIDS
LA English
EM 199509
AB Several assays can be used to identify HIV-1 integrase inhibitors. We are using recombinant HIV-1 integrase and radiolabeled oligonucleotides to study various reactions of HIV-1 integrase: DNA binding, 3'-processing, strand transfer, and disintegration. The disintegration reaction offers the advantage of being catalyzed by truncated integrase lacking the N-terminus (**zinc** finger) and the C- terminus (DNA binding) regions. Inhibition of the truncated enzyme suggests that the drugs act with the catalytic site of HIV-1 integrase. A number of inhibitors have been discovered using in vitro assays. They belong to three main categories: DNA binders, polyhydroxylated aromatic compounds, and nucleotides. Polyhydroxylated aromatic compounds are common in various plants. Many derivatives are available as natural or synthetic compounds. We have performed structure-activity relationships with flavones, lignans, and caffeic acid phenethylester (CAPE) derivatives CAPE is a main component of Propolis that bees use to reduce the size of the entrance and seal holes in their hives. Some of the synthetic derivatives are 10-fold more potent than CAPE and exhibit some activity in the anti-AIDS Screen of the National Cancer Institute. Based on drug structure and activity against the core HIV-1 integrase, we speculate that polyhydroxylated compounds and derivatives of phenanthroline cuprous complexes react with the conserved acidic amino acid that probably constitute the metal and polynucleotide binding site (DD[35]E). A variety of polyhydroxylated compounds from natural source are being investigated to discover lead structures with both anti- integrase and anti-viral activities. Nucleotides such as **AZT**-MP also inhibit purified HIV-1 integrase probably by binding to the polynucleotide binding site. Examples of sugar substituted nucleotides, polynucleotides and analogs with greater activity will be discussed. HIV-1 integrase inhibitors with antiviral activity are being actively searched as part of the NCI Antiviral Program and elsewhere. The **combined** administration of inhibitors of HIV-1 integrase, reverse transcriptase and/or protease may reduce the risk of acquired resistance during the treatment of HIV infections and AIDS.

CT Binding Sites
Catalysis
Drug Design
*DNA Nucleotidyltransferases: AI, antagonists & inhibitors
DNA Nucleotidyltransferases: ME, metabolism
DNA, Viral: ME, metabolism
Enzyme Inhibitors: CH, chemistry
*Enzyme Inhibitors: PD, pharmacology
*HIV-1: EN, enzymology
Nucleotides: CH, chemistry
Nucleotides: PD, pharmacology
Structure-Activity Relationship
CN EC 2.7.7.- (Integrase); 0 (DNA, Viral); 0 (Enzyme Inhibitors); 0 (Nucleotides)

L165 ANSWER 9 OF 20 AIDSLINE
AN 1995:7441 AIDSLINE
DN MED-95248387
TI Access to therapy in the Multicenter AIDS Cohort Study, 1989-1992.
AU Graham N M; Jacobson L P; Kuo V; Chmiel J S; Morgenstern H; Zucconi S L
CS Department of Epidemiology, Johns Hopkins University, School of Hygiene and Public Health, Baltimore, MD 21205, USA.
NC UO1-AI-35039 (NIAID)
UO1-AI-35040 (NIAID)
UO1-AI-35041 (NIAID)
+
SO JOURNAL OF CLINICAL EPIDEMIOLOGY, (1994). Vol. 47, No. 9, pp. 1003-12.
Journal code: JCE. ISSN: 0895-4356.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
FS MED; Priority Journals
LA English
OS MEDLINE 95248387
EM 199508
AB The study aims were (i) to describe secular trends in the utilization of antiretrovirals, antivirals, Pneumocystis carinii pneumonia (PCP) prophylaxis, and antifungal prophylaxis and (ii) to determine whether factors such as clinical status, health services utilization, insurance status, income, education and race were associated with access to therapy. Data on utilization of therapy, health services utilization, income and insurance status were collected semiannually from October 1990 through March 1992 from 1415 homosexual/bisexual HIV-1 seropositive men in the Multicenter AIDS Cohort Study (MACS). Prevalence of therapy use according to level of immunosuppression was determined at each study visit. Clinical AIDS was defined using the 1987 CDC definition. Factors associated with use of antiretroviral therapy and PCP prophylaxis were assessed using multiple logistic regression with robust variance techniques to adjust variance estimates and significance levels for within-person correlations of drug use over time. Prevalence of **zidovudine** use remained relatively constant throughout the study period. In contrast, use of **didanosine** (21-34%), acyclovir (23-34%) and dideoxycytidine (**zalcitabine**) (8-25%) increased in participants with clinical AIDS. Similar trends were seen for **combination** antiretroviral therapy, trimethoprim-sulfamethoxazole, dapsone, **ketoconazole** and fluconazole. However, reported use of aerosolized pentamidine fell. After adjusting for CD4+ lymphocyte count and HIV-1 symptoms, previous HIV-related hospitalization (OR = 1.52; 95% CI = 1.22-1.91), outpatient

visit (OR = 2.83; 95% CI = 2.12-3.78), having insurance (OR = 1.32; 95% CI = 1.01-1.75), college education (OR = 1.42; 95% CI = 1.13-1.80) and white race (OR = 1.58; 95% CI = 1.21-2.07) were all associated with being on antiretroviral therapy in persons without clinical AIDS. In persons with clinical AIDS, having insurance (OR = 2.89; 95% CI = 1.04-8.02) and a previous outpatient visit (OR = 11.69; 95% CI = 1.77-77.30) were the significant variables. Factors significantly associated with being on PCP prophylaxis in multivariate models were previous hospitalization, previous outpatient visit, and college education (for subjects without clinical AIDS.

CT Check Tags: Human; Male; Support, U.S. Gov't, P.H.S.
*Acquired Immunodeficiency Syndrome: TH, therapy
Adult
Antiviral Agents: TU, therapeutic use
Cohort Studies
*Health Services Accessibility
Hospitalization: SN, statistics & numerical data
Income
Insurance, Health: UT, utilization
Pneumonia, Pneumocystis carinii: PC, prevention & control
Racial Stocks
United States

CN 0 (Antiviral Agents)

L165 ANSWER 10 OF 20 AIDSLINE
AN 1994:13201 AIDSLINE
DN ICA10-94371365
TI Cutaneous histoplasmosis and cryptococcosis in AIDS patients.
AU Gan A T; Gangaram H B; Suraiya H H; Ganesapillai T
CS Department of Dermatology, Kuala Lumpur Hospital, Malaysia.
SO Int Conf AIDS, (1994). Vol. 10, No. 2, pp. 184 (Abstract No. PB0751).
CY Japan
DT (MEETING ABSTRACTS)
FS ICA10
LA English
EM 199412
AB Opportunistic deep cutaneous fungal infection may occur in AIDS patients. We report a patient with cutaneous histoplasmosis and another with cutaneous cryptococcal infection. The first patient, a 32 year old man with AIDS presented with a generalised non-pruritic eruption starting as papules which later became pustules and umblicated nodules. He was on cotrimoxazole and **ketoconazole** for pneumocystis carinii pneumonia and oesophageal candidiasis as well as **zidovudine**. Tissue culture grew Histoplasma species with a positive serum Histoplasma antibody. His skin lesions improved with itraconazole. However he succumbed to his deteriorating general condition. The second patient, a 32 year old man with AIDS was on **zidovudine** and cotrimoxazole for pneumocystis carinii pneumonia. He presented with pruritic vesiculo-papular erythematous lesions on his face, neck and limbs. Culture of lesional tissue and fluid isolated Cryptococcus neoformans. The serum cryptococcal antigen was however negative. He improved on fluconazole after initial failure to **ketoconazole** treatment. The classical treatment for cutaneous histoplasmosis and cryptococcosis is amphotericin B and 5-flucytosine. However, because of their toxicity, newer antifungals like itraconazole and fluconazole are replacing them in the management of these fungal infections in AIDS patients.
CT Check Tags: Case Report; Human; Male
Acquired Immunodeficiency Syndrome: DT, drug therapy
Adult

*AIDS-Related Opportunistic Infections: DI, diagnosis
AIDS-Related Opportunistic Infections: DT, drug therapy
Cryptococcosis: CO, complications
*Cryptococcosis: DI, diagnosis
Cryptococcosis: DT, drug therapy
Dermatomycoses: CO, complications
*Dermatomycoses: DI, diagnosis
Dermatomycoses: DT, drug therapy
Fluconazole: TU, therapeutic use
Histoplasmosis: CO, complications
*Histoplasmosis: DI, diagnosis
Histoplasmosis: DT, drug therapy
Itraconazole: TU, therapeutic use
Pneumonia, Pneumocystis carinii: CO, complications
Pneumonia, Pneumocystis carinii: DT, drug therapy
Trimethoprim-Sulfamethoxazole **Combination**: TU, therapeutic use
Zidovudine: TU, therapeutic use
RN 30516-87-1 (**Zidovudine**); 8064-90-2 (Trimethoprim-Sulfamethoxazole **Combination**); 84625-61-6 (Itraconazole); 86386-73-4 (Fluconazole)

L165 ANSWER 11 OF 20 AIDSLINE
AN 1994:8803 AIDSLINE
DN MED-94296419
TI Inhibition of 3'azido-3'deoxythymidine-resistant HIV-1 infection by **dehydroepiandrosterone** in vitro.
AU Yang J Y; Schwartz A; Henderson E E
CS Department of Microbiology and Immunology, Temple University School of Medicine, Philadelphia 19140.
NC R01 AI28761 (NIAID)
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1994). Vol. 201, No. 3, pp. 1424-32.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals; Cancer Journals
LA English
OS MEDLINE 94296419
EM 199410
AB Human immunodeficiency virus type 1 (HIV-1) isolated from patients with acquired immunodeficiency syndrome (AIDS) shows resistance to 3'azido-3'deoxythymidine (**AZT**) after one or two years of treatment. **AZT** also has significant toxic side effects, further limiting its use in the therapy of HIV-1-infected individuals. **Dehydroepiandrosterone** (**DHEA**) has been shown to have a broad spectrum of biological functions, to be bioavailable orally and to be relatively nontoxic. Epidemiological studies provide evidence that reduced serum levels of **DHEA** are related to the progression of AIDS in HIV-1 infection. **DHEA** has also been shown to inhibit HIV-1 replication in vitro and block HIV-1 reactivation from chronically infected cell lines. However, there have been no reports on the ability of **DHEA** to inhibit the replication of **AZT**-resistant strains of HIV-1. We investigated whether **DHEA** treatment could inhibit replication of **AZT**-resistant strains of HIV-1. Addition of **DHEA** to MT-2 cell cultures infected with either **AZT**-sensitive or **AZT**-resistant isolates of HIV-1 resulted in dose-dependent inhibition of HIV-1-induced cytopathic effect and suppression of HIV-1 replication as measured by accumulation of reverse transcriptase activity. At a concentration as low as 50 microM,

DHEA reduced **AZT**-resistant HIV-1 replication over 50 percent as measured by cytopathic effect and accumulation of reverse transcriptase activity. This study provides evidence that **DHEA** can inhibit the replication of **AZT**-resistant as well as wild-type HIV-1. Since the main targets for **DHEA** are metabolic and cellular signaling pathways leading to HIV-1 replication-activation, **DHEA** should be effective against multidrug-resistant strains of HIV-1. **Combined** with recently discovered immunoregulatory properties, the finding that **DHEA** is able to inhibit replication of both wild-type and **AZT**-resistant HIV-1 suggests that in vivo **DHEA** may have a much broader spectrum of action than originally anticipated.

CT Check Tags: Human; In Vitro; Support, U.S. Gov't, P.H.S.
Cytopathogenic Effect, Viral
Drug Resistance, Microbial
*HIV Infections: PC, prevention & control
*HIV-1: DE, drug effects
HIV-1: GD, growth & development
***Prasterone**: PD, pharmacology
Tumor Cells, Cultured
Virus Replication: DE, drug effects
***Zidovudine**: PD, pharmacology

RN 30516-87-1 (**Zidovudine**); **53-43-0 (Prasterone)**

L165 ANSWER 12 OF 20 AIDSLINE
AN 1994:6020 AIDSLINE
DN MED-94200324
TI Amelioration of azidothymidine-induced erythroid toxicity by hemin and stem cell factor in immune-suppressed mice.
AU Hamburger A W; Chen R B
CS University of Maryland Cancer Center/Department of Pathology, Baltimore 21201.
NC 1RO1 HL42069-01 (NHLBI)
SO EXPERIMENTAL HEMATOLOGY, (1994). Vol. 22, No. 4, pp. 348-52.
Journal code: EPR. ISSN: 0301-472X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals; Cancer Journals
LA English
OS MEDLINE 94200324
EM 199407
AB Recombinant cytokines such as stem cell factor (SCF) are currently being tested for the ability to ameliorate 3'azido-3'deoxythymidine (**AZT**)-induced anemia in AIDS patients. Recently, we showed that SCF greatly increased burst-forming units-erythroid (BFU-E) but failed to increase hematocrits of **AZT**-treated immune-deficient (MAIDS) mice. We reasoned that hemin, previously shown to both enhance BFU-E proliferation and accelerate erythroid maturation, might bring about differentiation of this large SCF-induced pool of BFU-E and further protect BFU-E from **AZT**'s toxic effect. We therefore studied, in vitro, the effect of **combinations** of hemin and SCF on growth of BFU-E from MAIDS mice. Hemin, at concentrations of 10 to 100 microM, ameliorated the growth-inhibitory effect of **AZT**. 50 microM hemin increased the ED50 of **AZT** from 1 x 10(-7) M to 1.7 x 10(-6) M. SCF also ameliorated **AZT**-induced toxicity, but to a lesser extent. SCF and hemin increased the number of BFU-E colonies observed in the presence of **AZT** in an additive fashion. The resistance of BFU-E to **AZT**'s cytotoxic effect was greater in cultures receiving hemin and SCF together than in cultures receiving SCF or hemin alone. **Zinc**

and tin protoporphyrins (Zn and Sn PP) increased the numbers of BFU-E observed. However, neither **zinc** nor tin protoporphyrins increased the ED50 of **AZT**. **Combinations** of SCF and hemin may prove useful in ameliorating **AZT** toxicity in both immune-suppressed mice and human immunodeficiency virus (HIV)-infected patients.

CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
*Erythropoiesis: DE, drug effects
*Hematopoietic Cell Growth Factors: PD, pharmacology
Heme: PD, pharmacology
*Hemin: PD, pharmacology
Mice
Mice, Inbred C57BL
Murine Acquired Immunodeficiency Syndrome: BL, blood
Murine Acquired Immunodeficiency Syndrome: DT, drug therapy
***Zidovudine**: AI, antagonists & inhibitors
RN 14875-96-8 (Heme); 16009-13-5 (Hemin); 30516-87-1 (**Zidovudine**)
CN 0 (Hematopoietic Cell Growth Factors); 0 (Stem Cell Factor)

L165 ANSWER 13 OF 20 AIDSLINE
AN 1993:12581 AIDSLINE
DN ICA9-93335840
TI Relationship between steady-state plasma concentrations of atovaquone (C55) and the use of various concomitant medications in AIDS patients with Pneumocystis carinii pneumonia.
AU Sadler B M; Blum M R
CS Burroughs Wellcome Co. Research Triangle Park, North Carolina.
SO Int Conf AIDS, (1993). Vol. 9, No. 1, pp. 504 (Abstract No. PO-B31-2213).
CY GERMANY: Germany, Federal Republic of
DT (CLINICAL TRIAL)
(MEETING ABSTRACTS)
FS ICA9
LA English
EM 199311
AB A multivariate analysis was performed to examine the associations between C55 and the use of a variety of concomitant medications in 191 patients participating in two efficacy trials of atovaquone. While a significant association between C55 and any particular medication would not, in itself, prove that a drug interaction had taken place, the lack of an association would be strong evidence that a drug interaction had not taken place. The purpose of this analysis was to identify drugs that would not reduce the plasma concentration (and presumably the therapeutic effect) of atovaquone when given in **combination**. Using stepwise multiple linear regression techniques, 13 of the 24 drugs (or drug classes), **zidovudine**, U plasma protein binders, clofazimine, antacids, erythromycin, clotrimazole, nonsteroidal antiinflammatory agents, **ketoconazole**, hydroxyzine, megesterol, antiemetics, other systemic steroids, and H2 antagonists, were not associated with a significant ($p > 0.15$) change in C55. However, four of these, **zidovudine**, erythromycin, clotazimine, and the U plasma protein binders were represented by five or fewer subjects. The expected C55 normalized for plasma albumin concentration, body weight, and no concomitant medications, was 14.8 micrograms/mL. Fluconazole and prednisone were associated with a significant increase in C55 (2.5 and 2.3 micrograms/mL, respectively). Acetaminophen, acyclovir, opiates, antidiarrheals, cephalosporins, benzodiazepines, and laxatives, were associated with significant decreases in C55 < or = 3.4 micrograms/mL. Metoclopramide and rifampin were associated with decreases of 7.2 and 7.8 micrograms/mL, respectively. Demographic variables for gender and race were not significant.

CT Check Tags: Female; Human; Male
Analgesics: PK, pharmacokinetics
Anti-Infective Agents: PK, pharmacokinetics
Anti-Inflammatory Agents, Non-Steroidal: PK, pharmacokinetics
Antidiarrheals: PK, pharmacokinetics
Antiemetics: PK, pharmacokinetics
*Antifungal Agents: BL, blood
Antifungal Agents: PK, pharmacokinetics
Antifungal Agents: TU, therapeutic use
*AIDS-Related Opportunistic Infections: DT, drug therapy
Cathartics: PK, pharmacokinetics
Drug Interactions
Histamine H2 Antagonists: PK, pharmacokinetics
Multivariate Analysis
*Naphthoquinones: BL, blood
Naphthoquinones: PK, pharmacokinetics
Naphthoquinones: TU, therapeutic use
*Pneumonia, Pneumocystis carinii: DT, drug therapy
Regression Analysis
Steroids: PK, pharmacokinetics
RN 94015-53-9 (atovaquone)
CN 0 (Analgesics); 0 (Anti-Infective Agents); 0 (Anti-Inflammatory Agents, Non-Steroidal); 0 (Antidiarrheals); 0 (Antiemetics); 0 (Antifungal Agents); 0 (Cathartics); 0 (Histamine H2 Antagonists); 0 (Naphthoquinones); 0 (Steroids)

L165 ANSWER 14 OF 20 AIDSLINE
AN 1993:388 AIDSLINE
DN MED-93010360
TI 3'-azido-3'-deoxythymidine drug interactions. Screening for inhibitors in human liver microsomes.
AU Rajaonarison J F; Lacarelle B; Catalin J; Placidi M; Rahmani R
CS Institut National de la Sante et de la Recherche Medicale, Marseille, France.
SO DRUG METABOLISM AND DISPOSITION, (1992). Vol. 20, No. 4, pp. 578-84. Journal code: EBR. ISSN: 0090-9556.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals
LA English
OS MEDLINE 93010360
EM 199301
AB **Zidovudine** is a widely used antiretroviral drug active against human immunodeficiency virus. The drug interactions of this compound, which are primarily eliminated as a glucuronide, have not yet been extensively studied. Because **zidovudine** is frequently **combined** with other drugs, complete knowledge of interactions is essential to optimize AIDS therapy. We therefore screened the effect of 55 molecules, representative of 20 different therapeutic classes, on 3'-azido-3'-deoxythymidine (**AZT**) glucuronidation by human liver microsomes. We demonstrate that many drugs caused more than 15% inhibition of **AZT** glucuronidation in vitro, whereas major antibiotics (ceftazidine, isoniazid, aminoglycosides, macrolides, and sulfamides), antivirals (2',3'-dideoxycytidine, 2',3'-dideoxyinosine, and acyclovir), flucytosine, metronidazole, acetaminophen, and ranitidine had no effect. For compounds that appeared to inhibit **AZT** glucuronidation, extrapolation to the clinical situation must take into account both the in vitro apparent Ki values and the usual expected plasma level for the coadministered drug. By considering these parameters, this work indicates

that clinically relevant inhibition of **AZT** glucuronidation may be observed with the following drugs: cefoperazone, penicillin G, amoxicilin, piperacillin, chloramphenicol, vancomycin, miconazole, rifampicin, phenobarbital, carbamazepine, **phenytoin**, valproic acid, quinidine, phenylbutazone, ketoprofen, probenecid, and propofol. Complementary clinical and pharmacokinetic studies should be performed to validate these assumptions.

CT Check Tags: Human; In Vitro
Drug Interactions
Kinetics
*Microsomes, Liver: ME, metabolism
***Zidovudine**: AA, analogs & derivatives
***Zidovudine**: ME, metabolism

RN 117675-21-5 (3'-azido-3'-deoxy-5'-O-beta-glucopyranuronosylthymidine); 30516-87-1 (**Zidovudine**)

L165 ANSWER 15 OF 20 AIDSLINE
AN 1992:16879 AIDSLINE
DN MED-92321680
TI Chemotherapy of murine colorectal carcinoma with cisplatin and cisplatin plus 3'-deoxy-3'-azidothymidine.
AU Klann R C; Holbrook C T; Nyce J W
CS Department of Pediatric Hematology, School of Medicine, East Carolina University, Greenville, NC 27858-4354.
SO ANTICANCER RESEARCH, (1992). Vol. 12, No. 3, pp. 781-7.
Journal code: 59L. ISSN: 0250-7005.
CY Greece
DT Journal; Article; (JOURNAL ARTICLE)
FS MED; Priority Journals; Cancer Journals
LA English
OS MEDLINE 92321680
EM 199210
AB In light of the discouraging results obtained with conventional chemotherapy of human colon cancer using 5-fluorouracil, we examined the effects of cis-diamminedichloroplatinum (cisplatin) alone and **combined** with 3'-deoxy-3'-azidothymidine (**AZT**) on chemotherapy of colorectal adenocarcinomas induced by dimethyldrazine in CD-1 mice. Thirteen weeks after a 20 week tumor induction period (15 mg/kg dimethylhydrazine weekly) groups of 19 mice were given either no therapy, or weekly cisplatin (6 mg/kg for 4 wks), **AZT** (400 mg/kg, wks 3 and 4), or cisplatin and **AZT**. Animals were autospied at death or after euthanasia on day 99 post initiation of therapy, their colons excised, fixed in buffered formalin and the number and volume of tumors measured. Cisplatin alone or with **AZT** decreased tumor size by 47-52%, and enhanced survival, leaving 55% of the mice alive at day 99 compared to 18% in controls. These therapeutic effects were amplified when animals were given chemotherapy during recovery from the effects of short-term dietary provision of the anti-carcinogenic steroid, **dehydroepiandrosterone** (**DHEA**). Our results suggest cisplatin is an effective chemotherapeutic agent against colon cancer in this murine model, and warrant further studies of its interaction with **AZT** and **DHEA** in enhancing this effect.

CT Check Tags: Animal; Female; Male
Antineoplastic Agents: AD, administration & dosage
*Antineoplastic Agents: TU, therapeutic use
*Antineoplastic Agents, **Combined**: TU, therapeutic use
Cisplatin: AD, administration & dosage
*Cisplatin: TU, therapeutic use
Colonic Neoplasms: CI, chemically induced

*Colonic Neoplasms: DT, drug therapy
Dimethylhydrazines
Mice
Mice, Inbred Strains
***Prasterone**: TU, therapeutic use
Zidovudine: AD, administration & dosage
***Zidovudine**: TU, therapeutic use
RN 15663-27-1 (Cisplatin); 30516-87-1 (**Zidovudine**); **53-43-0 (Prasterone)**
CN 0 (Antineoplastic Agents); 0 (Antineoplastic Agents, **Combined**); 0 (Dimethylhydrazines)

L165 ANSWER 16 OF 20 AIDSLINE
AN 1992:15486 AIDSLINE
DN ICA8-92403652
TI An unusual isolated kidney localization of invasive Aspergillosis in an AIDS.
AU Weiss L; Piketty C; George F; Lavarde V; Kazatchkine M D
CS Unite d'Immunopathologie, Hopital Broussais, Paris, France.
SO Int Conf AIDS, (1992). Vol. 8, No. 3, pp. 146 (Abstract No. PuB 7585).
CY Netherlands
DT (MEETING ABSTRACTS)
FS ICA8
LA English
EM 199212
AB OBJECTIVE: We report a case of invasive aspergillosis (ASP) presenting as renal abscess in a patient with AIDS in the absence of specific risk factors for ASP. ASP appears to be uncommon in patients with AIDS. Risk factors including neutropenia, prolonged steroid therapy or Marijuana inhalation are present in 80% of the reported cases of disseminated Aspergillosis. CASE: A 30 year-old male was first admitted in March 1991 for a severe Pneumocystis carinii pneumonia as the first manifestation of HIV infection. The patient was homosexual with no story of drug addiction. He was treated with anti-pneumocystis drugs and a short course of steroids. He then received Dapsone and **Zidovudine**. CD4 cell count was 7 x 10(9)/1. The patient was readmitted in December 1991 with fever (39 degrees C) and macroscopic hematuria without lumbar pain. The abdominal CT scan revealed a large abscess involving the entire right kidney. The white blood cell count was 10(9)/1 with 72% neutrophils. A nephrectomy was immediately performed. Direct examination of the pus showed Aspergillus fumigatus as the sole pathogen. The same fungus was isolated in the sputum and urine. There were no signs of pulmonary involvement by conventional X-ray and CT scan. The search for Aspergillus antigen in blood and urine was negative; no antibodies were detected. Neutrophil functions assessed in vitro were normal. The patient was initially treated with Itraconazole (400 mg daily). Serum levels of Itraconazole were found to be under therapeutic ranges and the daily regimen was increased to 1000 mg. Since the patient was also receiving Dapsone, a possible interaction between these two drugs can not be ruled out. The evolution was marked by the persistence of aspergillus infection in the right flank. CONCLUSION: Aspergillus infections may occur more frequently in AIDS patients as a consequence of prolonged survival. Isolated kidney localizations have not been so far reported in the literature.
CT Check Tags: Case Report; Human; Male
Abscess: CO, complications
*Abscess: DI, diagnosis
Abscess: DT, drug therapy
Adult

Antifungal Agents: TU, therapeutic use
Aspergillosis: CO, complications
*Aspergillosis: DI, diagnosis
Aspergillosis: DT, drug therapy
*Aspergillus fumigatus
Aspergillus fumigatus: DE, drug effects
Combined Modality Therapy
HIV Seropositivity: CO, complications
*HIV Seropositivity: DI, diagnosis
HIV Seropositivity: DT, drug therapy
Ketoconazole: AA, analogs & derivatives
Ketoconazole: TU, therapeutic use
Kidney Diseases: CO, complications
*Kidney Diseases: DI, diagnosis
Kidney Diseases: DT, drug therapy
Nephrectomy
Opportunistic Infections: CO, complications
*Opportunistic Infections: DI, diagnosis
Opportunistic Infections: DT, drug therapy
RN **65277-42-1 (Ketoconazole)**; 84625-61-6 (Itraconazole)
CN 0 (Antifungal Agents)

L165 ANSWER 17 OF 20 AIDSLINE
AN 1991:12281 AIDSLINE
DN ICA7-3207691
TI Immunomodulating effects of nutrient therapy used in **combination** with **AZT**.
AU Priestley J
CS Search Alliance Community Research Initiative, Los Angeles, CA, USA.
SO Int Conf AIDS, (1991) Vol. 7, No. 2, pp. 201 (Abstract No. W.B.2076).
CY Italy
DT (MEETING ABSTRACTS)
FS ICA7
LA English
EM 199112
AB OBJECTIVE: Often, people with HIV disease become deficient in several important nutrients, even rather early in the course of their disease. We studied the immunomodulating effects of nutrients used in **combination** with **AZT** and other anti-viral drugs. METHOD: We followed 92 patients (88 homosexual men and 4 heterosexual women) in all stages of HIV disease, over a period of 9 to 24 months. Patient's ages were between 23 to 52, at entry, and initial T4 cell counts ranged from 2 to 653. All patients took therapeutic doses of supplements containing vitamin C, A, E, all the B vitamins, **zinc**, selenium and trace elements. All patients with fewer than 200 T4 cells took Bactrim DS, 3 times per week to prevent Pneumocystis pneumonia. Sixty-three patients entered the study taking standard dosages of **AZT**, 500 mg per day. During the course of the study, 10 patients discontinued their **AZT** due to intolerance. Complete laboratory assessment, including T4/T8 count, T4 cell percent, CBC, SMAC 24, P24 antigen and P24 antibody, was obtained from each patient every 3 to 6 months. RESULTS: Twenty-two subjects dropped out of the study or were disqualified because they did not adhere to the study. Overall, the remaining 70 patients had a 92% two-year survival rate. Over the 2 years of this study, a total of 6 subjects died. Four died from progressive Kaposi's Sarcoma which they had upon entry into the study. In addition, 6 subjects developed an AIDS-defining illness and 2 of these people subsequently died. The other 64 subjects did not show disease progression; their symptoms and laboratory data, especially T4 cell count, remained stable throughout the

study. On average, T4 cell counts either stabilized or increased, while P24 antigen levels decreased and P24 antibody production remained strong. Survival has been independent of initial T4 cell counts. CONCLUSIONS: Nutrients appear to have a positive impact on overall function and survival of HIV-infected people. Nutrient therapy also appears to enhance the effectiveness of **AZT**, and may act to reduce its side-effects. Nutrient supplements are indicated as adjunctive HIV therapy, and further study is warranted.

CT Check Tags: Female; Human; Male
Adjuvants, Immunologic
Adult
Combined Modality Therapy
Gene Products, gag: AN, analysis
HIV Antigens: AN, analysis
HIV Infections: CO, complications
HIV Infections: DH, diet therapy
*HIV Infections: DT, drug therapy
Lymphocyte Subsets
Middle Age
Pneumonia, Pneumocystis carinii: PC, prevention & control
Sarcoma, Kaposi: ET, etiology
Viral Core Proteins: AN, analysis
Zidovudine: AE, adverse effects
***Zidovudine**: TU, therapeutic use

RN 30516-87-1 (**Zidovudine**)

CN 0 (Adjuvants, Immunologic); 0 (Gene Products, gag); 0 (HIV Antigens); 0 (HIV Core Protein p24); 0 (Viral Core Proteins)

L165 ANSWER 18 OF 20 AIDSLINE

AN 1991:11277 AIDSLINE

DN ICA7-3215991

TI Relationship between treatment scheme and short hospital stay in AIDS patients without the use of **AZT**.

AU Revuelta-Herrera A; Tapia-Conyer R; Cuauhtli M; Sepulveda-Amor J

CS Conasida-Mexico D.F., Mexico.

SO Int Conf AIDS, (1991). Vol. 7, No. 2, pp. 221 (Abstract No. W.B.2159).

CY Italy

DT (MEETING ABSTRACTS)

FS ICA7

LA English

EM 199112

AB OBJECTIVE: To determine the best diagnostic and therapeutic plan for AIDS patients from those available in health institutions, without use of **AZT**. METHOD: During 1988 we reviewed 467 clinical records of all HIV+ patients treated between 1985 and 1988 in two hospitals: one hospital is part of the Social Security System and the other is a public hospital. We reviewed only the first admission. The information was obtained in a previously structured questionnaire which included record identifications, laboratory and office procedures, diagnosis other than AIDS, and prescribed drugs. We analyzed the statistical association between other diagnoses, diagnostic and therapeutic management reported by physicians, and short stays at hospital with improvement discharge. RESULTS: Ninety two percent of all patients were males and 8% females; 77% were at Ia and Ic categories according to the CDC's classification. Patient hospital stay was on the average, 19 days, and a mean of 26 laboratory tests were performed. The most frequent diagnosis in these patients was Tuberculosis (14%), Candida albicans (10%), and Pneumonia (14%), of the last diagnosis 45%, were Pneumocystis carinii. Fifty three percent of all patients received 10 drugs during their hospital stay, and 78% received up to 1-15

drugs in that period. We found a positive association between short stays and AIDS-tuberculosis patients treated with Isoniazid, Rifampicin and KCI; AIDS-Candida albicans patients treated with **ketoconazole**; and finally, AIDS-Pneumocystis carinii pneumonia patients treated with Trimethoprim-sulfamethoxazole (P less than 0.05). DISCUSSION AND CONCLUSIONS: In Mexico, not all AIDS patients can pay for **AZT** treatment, therefore we must search for better utilization of available resources in order to lessen the economic impact of AIDS and give patient better results.

CT Check Tags: Female; Human; Male
Acquired Immunodeficiency Syndrome: CO, complications
Acquired Immunodeficiency Syndrome: EC, economics
*Acquired Immunodeficiency Syndrome: TH, therapy
Candidiasis: CO, complications
Candidiasis: DT, drug therapy
Hospitals
Isoniazid: TU, therapeutic use
Ketoconazole: TU, therapeutic use
*Length of Stay
Pneumonia, Pneumocystis carinii: CO, complications
Pneumonia, Pneumocystis carinii: DT, drug therapy
Trimethoprim-Sulfamethoxazole **Combination**: TU, therapeutic use
Tuberculosis: CO, complications
Tuberculosis: DT, drug therapy
***Zidovudine**: TU, therapeutic use

RN 30516-87-1 (**Zidovudine**); 54-85-3 (Isoniazid); **65277-42-1 (Ketoconazole)**; 8064-90-2 (Trimethoprim-Sulfamethoxazole **Combination**)

L165 ANSWER 19 OF 20 AIDSLINE
AN 1991:8863 AIDSLINE
DN MED-91319495
TI Low-dose **zidovudine** in children with an human immunodeficiency virus type 1 infection acquired in the perinatal period [see comments].
CM Comment in: Pediatrics 1991 Aug;88(2):389-92
AU Blanche S; Duliege A M; Navarette M S; Tardieu M; Debre M; Rouzioux C; Seldrup J; Kouzan S; Griscelli C
CS Pediatric Immunology Division, Necker Hospital, Institut National de la Sante et de la Recherche Medicale U132, Paris, France.
SO PEDIATRICS, (1991). Vol. 88, No. 2, pp. 364-70.
Journal code: OXV. ISSN: 0031-4005.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
FS MED; Abridged Index Medicus Journals; Priority Journals
LA English
OS MEDLINE 91319495
EM 199111
AB This report describes the one-year results of a noncomparative study designed to assess the safety and tolerance of low-dose **zidovudine** (azidothymidine) given orally to 60 human immunodeficiency virus type 1-infected infants and children. At baseline, the mean age was 1.9 years (+/- 1.4), and all were symptomatic: 43% were P2A and 57% were P2B to F according to the Centers for Disease Control classification. All the patients received **zidovudine** for at least 6 months, and 52 of them (87%) completed a full year of therapy. The mean duration of follow-up was 346 days (+/- 42) (range, 183 to 366 days). The initial therapy consisted of four daily doses of 100 mg/m2 (400 mg/m2 per day, equivalent to 20 mg/kg per day). However, this treatment was modified when

neutropenia or anemia was observed. Twenty-nine children (48%) remained at the initial therapy for the entire study. **Zidovudine** dosage was adjusted 92 times in the other 31 children (52%), mostly due to neutropenia (83%). Altogether, the time under full-dose therapy represented 81% of the total duration of the protocol for all patients. Children with mild symptoms, P2A at study entry, were more likely to remain under full-dose therapy than children with severe symptoms, P2B to F: the time under full-dose therapy represented 91% of the duration of the protocol for the former group and only 74% for the latter one (P less than .02). No clinical adverse experiences were attributed directly to **zidovudine**. Thirty-seven children were prescribed trimethoprim-sulfametoxazole as a prophylaxis for Pneumocystis carinii pneumonia.(ABSTRACT TRUNCATED AT 250 WORDS)

CT Check Tags: Female; Human; Male
*Acquired Immunodeficiency Syndrome: DT, drug therapy
Child, Preschool
Drug Administration Schedule
Drug Tolerance
Immunization, Passive
Infant
Ketoconazole: TU, therapeutic use
Opportunistic Infections: PC, prevention & control
Trimethoprim-Sulfamethoxazole **Combination**: TU, therapeutic use
Zidovudine: AD, administration & dosage
Zidovudine: AE, adverse effects
***Zidovudine**: TU, therapeutic use

RN 30516-87-1 (**Zidovudine**); **65277-42-1 (Ketoconazole)**; 8064-90-2 (Trimethoprim-Sulfamethoxazole **Combination**)

L165 ANSWER 20 OF 20 AIDSLINE
AN 1990:11236 AIDSLINE
DN ICA5-00286089
TI Effect of **dehydroepiandrosterone** (**DHEA**) in lymphocytes and macrophages infected with HIV-1.
AU Schinazi R F; Eriksson B F; Aronld B; Lekas P; McGrath M S
CS Veterans Administration Med. Ctr, and Emory University Sch. of Med., Atlanta, Ga., USA.
SO Int Conf AIDS, (1989). Vol. 5, pp. 551 (Abstract No. M.C.P.55). ISBN: 0-662-56670-X.
CY Canada
DT (MEETING ABSTRACTS)
FS ICA5
LA English
EM 199009
AB OBJECTIVE: Since the spectrum of activity of **DHEA** and structural analogues against human retroviruses has not been reported, several in vitro studies were performed to determine the degree of antiviral selectivity and mechanism of action of these drugs. METHODS: The inhibition of HIV-1 multiplication in the various cells was determined by reverse transcriptase assay of disrupted virions obtained from culture medium or by a p24 assay. The methodologies have been described in detail (see Antimicrob. Agents Chemother. 33:115, 1989; 32:1784, 1988; 30:491, 1986). RESULTS: The ability of **DHEA** and 3'-azido-3'-deoxythymidine (**AZT**) to inhibit the replication of HIV-1 was examined in human peripheral blood mononuclear cells (PBMC). Reverse transcriptase (RT) activity associated with virus and the amount of HIV-1 p24 antigens in the supernatant were used to assess the antiviral activity. Using the former assay, the median effective concentrations for **DHEA** and **AZT** were 17 mu M and 0.0014 muM, respectively.

Results obtained by an enzyme immunoassay were similar. **DHEA** -sulfate was markedly less active than **DHEA**. In contrast, 16alpha-bromoepiandrosterone was more potent and also more toxic than **DHEA**. The specific antiviral activity of **DHEA** was confirmed in CEM cells. Although this steroid was still effective when added up to 3 days after infection, late treatment was not as effective as early treatment. **DHEA** did not have a direct virucidal effect on infectious virus. In contrast to the 5'-triphosphate of **AZT** and other known antiretroviral agents, **DHEA** did not inhibit HIV-1 RT enzymatic activity when tested up to 100 muM. Acute infection of normal human macrophages was also inhibited by **DHEA** at 10-100 muM. Multiple-drug effect analyses were used to quantitatively determine the interaction of **AZT** and **DHEA** in human PBMC infected with HIV-1 at a ratio of 1:1,000 and 1:4,000. Analyses of the cell culture data indicated mostly an antagonistic interaction. At therapeutic levels, no apparent toxicity to uninfected cells was observed. CONCLUSION: Our studies indicated that **DHEA** was a modest selective inhibitor of HIV-1 replication in human lymphocytes and macrophages. The mechanism(s) involved in the antiviral activity of **DHEA** and its sulfated form must be on sites other than the HIV-1 RT. In vitro results revealed that the **combination** of **AZT** and **DHEA** may decrease the efficacy of **AZT** or exacerbate virus replication.

CT Check Tags: Human
*Antiviral Agents: PD, pharmacology
Cells, Cultured
Gene Products, gag: AN, analysis
*HIV-1: DE, drug effects
HIV-1: IP, isolation & purification
HIV-1: PH, physiology
*Lymphocytes: MI, microbiology
*Macrophages: MI, microbiology
***Prasterone**: PD, pharmacology
RNA-Directed DNA Polymerase: ME, metabolism
Viral Core Proteins: AN, analysis
Virus Replication: DE, drug effects

RN **53-43-0 (Prasterone)**

CN EC 2.7.7.49 (RNA-Directed DNA Polymerase); 0 (Antiviral Agents); 0 (Gene Products, gag); 0 (HIV Core Protein p24); 0 (Viral Core Proteins)

=> d his l171-

(FILE 'WPIDS' ENTERED AT 14:13:11 ON 25 JUL 1999)
E PROCAINE/DCN
E E3+ALL/DCN
L171 359 S E2 OR 0186/DRN
E PROCAINE/DCN
E E4_ALL/DCN
E PROCAINE/DCN
E E4+ALL/DCN
L172 8 S E2 OR 3760/DRN
E PROCAINE/DCN
E E6+ALL/DCN
L173 170 S E2 OR 4423/DRN
L174 660 S L171-L173 OR PROCAINE
L175 9 S L174 AND (ZN OR ZINC)
L176 5 SEA L174 AND A430/M0,M1,M2,M3,M4,M5,M6
E R0305+ALL/DCN
E R030E5+ALL/DCN
E R03035+ALL/DCN

PA (SPEC-N) SPECTRUM PHARM CORP
CYC 1
PI US 5064858 A 911112 (9148)*
ADT US 5064858 A US 90-578030 900905
PRAI US 88-233247 880817; US 90-578030 900905
IC A61K009-14; A61K031-21
AB US 5064858 A UPAB: 19930928
The compsn. comprises **procaine** (1-10%), a complexing agent (e.g. 0.25-10% ascorbic acid) and opt. lidocaine, zinc citrate, an anticholinesterase, or an anticortisol agent (e.g. dilantin or clonidine), etc.. Other possible complexing agents are acetylsalicylic acid (for treating Alzheimer's disease), polysaccharides, glycols, pantothenic acid, amino acids and caffeine.

USE/ADVANTAGE - The compsn. is used to reduce the withdrawal symptoms of individuals addicted to narcotics or to treat the symptoms of age-related conditions such as tinnitus and Alzheimer's disease. It may be administered orally, parenterally or intravenously. An oral dosage unit contains 25-300 mg of **procaine**, and a parenteral dosage unit contains 25-100 mg of **procaine**.

In an example, 11 individuals having chronic and recurring addiction to cocaine are treated with a formulation comprising a protected complex of 4% **procaine** complexed with ascorbic acid. Dosage is 200-300 mg/day. After 3 weeks, 9 of the addicts avoid the use of cocaine or other narcotics for 3-7 months. Furthermore, attempts to use cocaine during the three-week period lead to aversion symptoms including vomiting, abdominal pain and muscle cramps. @(5pp Dwg.No.0/0)
FS CPI
FA AB; DCN
MC CPI: B03-F; B04-A06; B04-C02; B05-A03A; B07-D04A; B07-D09; B10-B01A; B10-B02; B10-C02; B10-C03; B10-C04D; B10-E04C; B12-C09; B12-G01B1; B12-G01B3; B12-G04; B12-J05; B12-L04

L187 ANSWER 3 OF 4 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1990-368149 [49] WPIDS
CR 92-365522 [44]
DNC C90-160235
TI Insulin potentiation therapy of viral infections and cancer - comprises admin. of insulin followed by combination of glucose and antiviral or anti neoplastic drug.
DC B04 B05
IN AYRE, S G; PEREZ, G; PEREZ, G Y B; BELLON, D G; GARCIA, D P
PA (AYRE-I) AYRE S G; (BELL-I) GARCIA D P & BELLON
CYC 2
PI US 4971951 A 901120 (9049)*
CA 1299102 C 920421 (9221) A61K037-26
ADT US 4971951 A US 88-77833 880727; CA 1299102 C CA 87-539603 870615
PRAI CA 87-539603 870615
IC ICM A61K037-26
AB US 4971951 A UPAB: 19931116
Viral diseases are treated by administration of, pref. 1 unit/kg body wt., insulin sufficient to induce hypoglycaemia followed by administration of glucose and an antiviral drug. Pref. the glucose is administered as 20-50 cc 50% hypertonic glucose solution. Specifically, the drug is cyclophosphamide, methotrexate, 5-fluoroacil, azidothymidine, ribavirin, surmarin or HPA-23. The method is pref. carried out on a weekly basis. Pharmaceutical compsns. are claimed which comprises insulin (1 unit/kg), glucose (20-50 cc) 50% solution and an antineoplastic agent or anti-AIDS drug. Administration is pref. intravenously.

USE/ADVANTAGE - Treatment of viral diseases, especially AIDS and

cancer. Insulin acts to increase cell membrane permeability thus potentiating the effects of the drug. @(6pp Dwg.No.0/0)@
0/0
FS CPI
FA AB; DCN
MC CPI: B04-B02D2; B04-B03A; B05-A02; B05-B01M; B06-D09; B10-A07; **B12-A06**; B12-G07

L187 ANSWER 4 OF 4 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1990-297515 [39] WPIDS
DNC C91-152308
TI Compsn. for treating addiction to narcotics - comprises protected complex of **procaine** and complexing agent such as ascorbic, pantothenic acetyl salicylic or aminoacid(s).
DC B05
IN **SAPSE, A T**
PA (SAPS-I) SAPSE A T
CYC 1
PI US 4956391 A 900911 (9039)*
ADT US 4956391 A US 88-233247 880817
PRAI US 88-233247 880817
IC A61K027-00
AB US 4956391 A UPAB: 19930928
Compsn. comprises **procaine** (I) and a complexing agent capable of forming a protected complex with (I), in amt. effective to reduce the withdrawal symptoms. The complexing agent comprises ascorbic, pantothenic, acetylsalicyclic or amine acids.
Pref. the compsn. further comprises lidocaine, zinc citrate, anticholinesterases and/or anticortisol agents. The anticortisol agent is dilantin and/or clonidine. Pref. amt. of (I) is 1-10 wt.%.
USE - The compsn. can also be used to treat tinnitus and Alzheimer's disease. @
0/0@
FS CPI
FA AB; DCN
MC CPI: B07-A01; B07-D09; B10-B01A; B10-B02; B10-C02; B10-C03; B10-C04D; B12-G01A; B12-G01B3; B12-G04A; B12-J05; B12-L04

=> d all tot l188

L188 ANSWER 1 OF 8 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1999-253224 [21] WPIDS
DNC C99-073950
TI New topical composition for the treatment of Rhus dermatitis.
DC B04 B05
IN ALBERT, B M; RISO, R R
PA (ALBR-N) ALBROS LP
CYC 1
PI US 5888515 A 990330 (9921)* 4 pp A61K035-78
ADT US 5888515 A US 97-989067 971211
PRAI US 97-989067 971211
IC ICM A61K035-78
ICS A61K031-045; A61K031-70; A61K047-00
AB US 5888515 A UPAB: 19990603
NOVELTY - New topical composition for the treatment of Rhus dermatitis comprises a mixture of jewelweed extract, plantain leaf extract and an aqueous colloidal dispersion of oat grains.
ACTIVITY - Dermatological; antiinflammatory; antipruritic; anaesthetic.

MECHANISM OF ACTION - None given.
USE - The composition is useful for the treatment and prevention of Rhus dermatitis (poison ivy).
ADVANTAGE - The components of the mixture have synergistic effects. The amphiphilic nature of the aqueous colloidal oat dispersion preserves the activity of the plantain jewelweed enzymes as a result of its oat oil fraction and also enhances topical delivery due to its aqueous fraction and the stabilising effect of the oat bran as a bulking agent. Skin layers are soothed, skin healing is promoted and pain and itching are minimised.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-A08C2; B04-A10B; B04-A10G; B14-C08; B14-G02A; B14-N17C; B14-S09

L188 ANSWER 2 OF 8 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1998-479346 [41] WPIDS
DNC C98-144905
TI Medicinal preparation against ageing - contains **procaine** hydrochloride aqueous and oil solution vitamin(s), metallic elements, and super oxide-dismutase.
DC B05
IN BARSAN, M M; BOTEZ, M
PA (BARS-I) BARSAN M M; (BOTE-I) BOTEZ M
CYC 1
PI RO 112997 B1 980330 (9841)* 1 pp A61K037-43
ADT RO 112997 B1 RO 97-28 970110
PRAI RO 97-28 970110
IC ICM A61K037-43
AB RO 112997 B UPAB: 19981014
A medicinal preparation against ageing contains (all parts by weight): 0.1-0.2 **procaine** hydrochloride; 50-200 superoxide-dismutase; 1.5-5 vitamin B2; 60-500 vitamin C; 10-100 vitamin B1; 20-200 vitamin B6, 10-30 vitamin PP; 400-1000 IU vitamin A; 10-30 IU vitamin E; 400-1200 IU vitamin D; 5-50 **Zn**; 2-5 Mn; 40-120 Ca; 200-400 Mg; 400-1200 P; 2-5 K; and 0.05-0.300 Se. The ingredients are formulated as tablets or solutions.
Dwg.0/0
FS CPI
FA AB
MC CPI: B03-L; B04-L03A; B05-A01A; B05-A01B; B05-A03A; B05-B02A3; B05-B02C; B10-B01A; B14-J01A4

L188 ANSWER 3 OF 8 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1997-550494 [51] WPIDS
DNC C97-175628
TI Ointment for treating skin diseases, e.g. hand or foot tinea or chapped skin.
DC B05
IN WANG, Z
PA (WANG-I) WANG Z
CYC 1
PI CN 1129111 A 960821 (9751)* A61K035-64
ADT CN 1129111 A CN 95-113050 951027
PRAI CN 95-113050 951027
IC ICM A61K035-64
ICS A61K009-06
AB CN 1129111 A UPAB: 19971222
Ointment (I) comprises **procaine**, queen-bee tonic, boric acid, triethanolamine, ortho- hydroxybenzoic acid, **zinc** oxide,

dexamethasone and vaseline.

USE - (I) is useful for the treatment of buttocks tinea, hand or food tinea, chapped skin, eczema of scrotum and eczema around anus and other skin diseases.

ADVANTAGE - (I) has a permanent and fast-acting effect. (I) contains reduced amounts of active ingredient, and has high curative effect without toxicity or side effects. The curative effect of (I) is not affected by geological differences, climate, water quality or callus quality.

FS CPI
FA AB
MC CPI: B01-B02; B04-B01C3; B04-B04M; B05-A03A; B05-B02C; B10-B01A; B10-B03B; B10-C03; B12-M02B; B14-A04C; B14-N17

L188 ANSWER 4 OF 8 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1994-157935 [19] WPIDS
DNC C94-072578
TI Wound sterilisation soln. with antiseptic activity - based on 'dioksidin', with additional **zinc** and cobalt sulphate(s), chymotrypsin and **procaine**.
DC B05
IN FEDORINA, A P
PA (POME-R) POLT MED STOMATOLOGY INST
CYC 1
PI SU 1799594 A1 930307 (9419)* 3 pp A61K009-08
ADT SU 1799594 A1 SU 90-4872459 900801
PRAI SU 90-4872459 900801
IC ICM A61K009-08
AB SU 1799594 A UPAB: 19940627
More effective local treatment of wounds infected with suppurative microorganisms.

The antiseptic prepn., namely 'diotsinkokhim' (sic), contains the following ingredients (wt.%): 'dioksidin' (sic) (0.05-0.1); **zinc** sulphate (0.11-0.44); cobalt sulphate (0.12-0.48); chymotrypsin (0.0005-0.01); **procaine** (0.25-0.5); distilled water (balance).

USE/ADVANTAGE - For treating suppurative and inflammatory processes or preventing development of suppuration in patients with soft or bony tissue injuries. Effective against a wide range of microorganisms, including those resistant to antibiotics and other antiseptics.
Dwg.0/0
FS CPI
FA AB
MC CPI: B05-A03; B10-A22; B14-A01; B14-N17B

L188 ANSWER 5 OF 8 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1994-157934 [19] WPIDS
DNC C94-072577
TI Castor oil-based lipstick compsn. having antiinflammatory and bacterial properties - contains additional light filter comprising extracts of coffee, propolis, daisy and hops..
DC B05 D21
IN BASKAKOVA, N M; OLILETS, M V; SHUKHMAN, M I
PA (STAL-R) STALGENE AGRIC FIRM AEROSOL ASSOC
CYC 1
PI SU 1799593 A1 930307 (9419)* 4 pp A61K007-027
ADT SU 1799593 A1 SU 90-4877675 900904
PRAI SU 90-4877675 900904
IC ICM A61K007-027
AB SU 1799593 A UPAB: 19940627
UV filtration is ensured through combined action of components.

The lipstick comprises the following components (wt%): perfumery oil (5.3-19.5); montan wax (5-9); beeswax (5-8); lanolin (5-10); petrolatum (2-6); paraffin (2-6); stearyl stearate (2-5); sorbitan oleate (1-5); silicone oil (2-5); isopropyl myristate (2-5); cacao butter (1-5); UV filter consisting of coffee fat and oil extract, mink oil propolis extract and carbonic acid extracts of daisy and hops in 1.5:1:1:1 ratio (3-5); mother-of-pearl paste (13.5-26.5); dye (0.5-7.0); perfume (1-1.7); castor oil (balance). Optimum light-filtration activity is manifested at 280-320 nm by virtue of the synergistic effects of the coffee, propolis, daisy and hops extracts.

USE/ADVANTAGE - Used in cosmetics industry for mfg decorative lip prods. The lipstick material exhibits antiinflammatory and bactericidal properties, and reduces allergenic reactions.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B04-A08C2; B04-A10; B04-B01C; B04-C03D; B10-G02; B14-A01; B14-C03; B14-S09; D08-B01

L188 ANSWER 6 OF 8 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1993-303017 [38] WPIDS
DNC C93-134897
TI New zaragozic acid derivs. - useful in treatment of arteriosclerosis, fungal infections and cancer.
DC B02 D16
IN ARISON, B H; BYRNE, K M; CHEN, S T; KAPLAN, L; MACCONNELL, J G; OMSTEAD, M N; PETUCH, B R; WHITE, R F; MAC, CONNELL J G
PA (MERI) MERCK & CO INC
CYC 40
PI WO 9317557 A1 930916 (9338)* EN 76 pp A01N043-32
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AU BB BG BR CA CZ FI HU JP KR LK MG MN MW NO NZ PL RO RU SD SK UA US
US 5252471 A 931012 (9342) 7 pp C12P017-18
AU 9337969 A 931005 (9405) A01N043-32
US 5294627 A 940315 (9411) 9 pp A61K031-335
US 5302604 A 940412 (9414) A61K031-38
ADT WO 9317557 A1 WO 93-US2095 930308; US 5252471 A US 92-848573 920309; AU 9337969 A AU 93-37969 930308; US 5294627 A US 92-936708 920827; US 5302604 A CIP of US 92-848628 920309, US 92-957316 921006
FDT AU 9337969 A Based on WO 9317557
PRAI US 92-848573 920309; US 92-848628 920309; US 92-936708 920827; US 92-957316 921006
REP EP 450812; S 5026554 US; 5053425 US 5; 055487 US 50; 96923 US 510; 2907 US 5200
IC ICM A01N043-32; A61K031-335; A61K031-38; C12P017-18
ICS A01N043-54; A61K031-44; A61K031-505; C07D319-08; C07D493-08; C12N001-14
AB WO 9317557 A UPAB: 19931123
Zaragozic acid derivs. of formula (I) and (II), and their salts, are new. In (I) T is C(=CH2)(in I) or CH2(in (II)); T' is a gp. of formula (a) (in (I)) or a gp. of formula (b) (in (II); R1 is a gp. of formula (iii)-(vi); X is H, halo, OH or Mr; Y is halo, OH or Me; Z1-Z3 are H or 1-5C alkyl (opt. substd. by phenyl (itself opt. monosubstd. by Me, MeO, halo or OH), or a gp. Q (which opt. form a 5-10 membered mono- or bicyclic ring with 1-5C alkyl) or a gp. of formula (vii) or (viii); and Q is 1-5C alkyl-carbonyloxy, 5-10C aryl-carbonyloxy, 1-5C alkyl-carbonyloxy or 6-10C aryl-carbonyloxy.

USE/ADVANTAGE - The new cpds. are squalene synthase inhibitora and

are useful as cancer treatment agents, cholesterol lowering agents and antifungal agents. They may be used e.g. to treat arteriosclerosis, hyperlipidaemia, familial hypercholesterolarmia, etc. They may be administered in combination with HMG-CoA reductase inhibitors, HMG-CoA synthase inhibitors, squalene epoxidase inhibitors, protincol, niacin, gemfibrozil, clofibrate, LDL-receptor gene inducers, etc. Asmin. is oral or parenteral in doses of 20-2000 mg/day.
30
Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: B06-A02; B12-A02C; B12-G01B1; B12-G07; B12-H03; D05-C

L188 ANSWER 7 OF 8 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1993-218204 [27] WPIDS
DNN N93-167211 DNC C93-097251
TI Treatment of duodenal ulcers in women - involves electrophoresis over appendage area using copper sulphate soln. during first phase of menstrual cycle, and **zinc** sulphate during second phase.
DC B05 B06 P34 S05
IN GANTSEV, SH KH; PRAZDNIKOV, E N; SAKHAUTDINOV, V G
PA (SAKH-I) SAKHAUTDINOV V G
CYC 1
PI SU 1745267 A1 920707 (9327)* 4 pp A61N001-34
ADT SU 1745267 A1 SU 90-4780046 900111
PRAI SU 90-4780046 900111
IC ICM A61N001-34
AB SU 1745267 A UPAB: 19931116
Electrophoresis is carried out over the appendage area using copper sulphate soln. during the first phase of the menstrual cycle, and electrophoresis of 2% soln. of **zinc** sulphate altered in a day with endo-nasal electrophoresis of 2% soln. of Novocaine during second phase of the menstrual cycle. Treatment is started not later than 2-4 days before supposed ovulation, and is carried out for 18-20 days.
USE/ADVANTAGE - In gastroenterology. Higher therapeutical efficiency and longer remission time are obtd. by normalising the hormonal profile of female sex hormones. Bul.25/7.7.92
Dwg.0/0
FS CPI EPI GMPI
FA AB; DCN
MC CPI: B05-A03A; B10-B01A; B12-G04; B12-J01
EPI: S05-A04

L188 ANSWER 8 OF 8 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1992-249386 [30] WPIDS
DNC C92-111273
TI Sterile injectable mixt. for tumour thermotherapy - useful for intense and local radio frequency, contg. ferrite plastic coated insol particles.
DC A96 B07
IN LEVEEN, E G; LEVEEN, H H; LEVEEN, R F
PA (THER-N) THERMAL DEV INC
CYC 1
PI US 5128147 A 920707 (9230)* 3 pp A61K009-16
ADT US 5128147 A Cont of US 89-294005 890106, US 90-563206 900806
PRAI US 89-294005 890106; US 90-563206 900806
IC ICM A61K009-16
ICS A61K009-50; A61K033-26; A61K033-32
AB US 5128147 A UPAB: 19931006
Mixt. comprises a combination of finely ground manganese **zinc**